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Review Article

Impact of Myocardial Bridging on Cardiac Function, Symptoms and Prognosis in Coronary Artery Disease; a Systematic Review

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Abstract

Myocardial bridging (MB) is a congenital anomaly characterized by the tunneled course of a coronary artery through the myocardium. Although generally considered a benign condition, MB has been associated with various clinical manifestations, including angina pectoris, myocardial infarction, and even sudden cardiac death. This systematic review aims to provide an updated understanding of MB with focus on its association with coronary artery disease, also encompassing its pathophysiology, clinical presentation, diagnosis, and management. The review discusses the complex interplay between hemodynamic forces, coronary artery compression, and the resulting myocardial ischemia. It explores the clinical spectrum of MB, ranging from asymptomatic individuals to those presenting with exertional chest pain or acute coronary syndromes. Diagnostic modalities, including invasive coronary angiography, intravascular ultrasound, and computed tomography angiography, are critically evaluated in light of their strengths and limitations. Furthermore, the review sheds light on the management strategies for patients with MB, including medical therapy, percutaneous coronary intervention, and surgical options. In conclusion, this review provides an updated and comprehensive overview of MB, emphasizing the importance of early recognition, accurate diagnosis, and tailored management strategies for optimizing patient outcomes.

Introduction

Myocardial bridging is a structural anomaly of the coronary arteries that has gained significant attention in the field of cardiology. It is characterized by the tunneled course of a segment of the coronary artery within the myocardium [1]. While often considered a benign condition, myocardial bridging has been associated with various clinical manifestations and poses a diagnostic and therapeutic challenge.

The pathophysiology of myocardial bridging involves the compression of the coronary artery during systole due to the contractile forces of the overlying myocardial bridge. This leads to a reduction in coronary blood flow, resulting in myocardial ischemia and potential clinical symptoms. The exact mechanisms underlying the development of myocardial bridging are not yet fully understood, but it is believed to arise from a combination of genetic predisposition and anatomical variations [2]. Clinical presentation of myocardial bridging can vary widely, ranging from asymptomatic cases to those with significant cardiac symptoms, including exertional angina, acute coronary syndrome, and even sudden cardiac death. The diagnosis of myocardial bridging is primarily based on invasive coronary angiography, although non-invasive imaging modalities such as computed tomography angiography and intravascular ultrasound have emerged as valuable tools for assessment.

In this systematic review, we aim to review the existing literature to provide an up-to-date overview of myocardial bridging, focusing on its association with coronary artery diseases and its pathophysiology, common clinical presentation, diagnostic approaches, and management strategies. We will explore the latest research findings, including epidemiological data, risk factors, and the association of myocardial bridging with other cardiovascular conditions. Furthermore, we will discuss the challenges encountered in the evaluation and treatment of myocardial bridging, highlighting the importance of individualized patient management especially when complicated by its association with coronary artery disease.

By enhancing our understanding of myocardial bridging and its implications, this review seeks to contribute to the advancement of clinical knowledge and facilitate evidence-based decision-making for healthcare professionals managing patients with this unique coronary artery anomaly.

Methods

We conducted a systematic review of three electronic databases, PubMed, MEDLINE (included within PubMed search), and Scopus. We searched the databases between June 18th, 2020 to June 27th, 2023. Our search strategy was according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.

Research question

Our research questions are listed as follows

1. How does and to what extent does myocardial bridging impact cardiac function in coronary artery disease patients?
2. What are the symptoms in patients with coronary artery disease and myocardial bridging?
3. What is the prognosis of patients with coronary artery disease and myocardial bridging?
4. Any noticed gender differences?

Keywords were selected using the PCC framework (Participant, context, concept). (Table 1) shows the keywords used along with Boolean operators.

	Main keyword	Alternate keywords
Participant	Coronary artery disease	Ischemic heart disease Coronary heart disease
Concept	Myocardial bridging	
Context	Cardiac function Symptoms Prognosis	Ejection fraction
Search strategy	(Participant keywords) AND (Concept keywords) AND (context keywords)	Search 1: (“Coronary artery disease” OR “Ischemic heart disease” OR “coronary heart disease”) AND (“Myocardial bridging”) Search 2: (“Coronary artery disease” OR “Ischemic heart disease” OR “coronary heart disease”) AND (“Myocardial bridging”) AND (“Symptoms”) Search 3: (“Coronary artery disease” OR “Ischemic heart disease” OR “coronary heart disease”) AND (“Myocardial bridging”) AND (“cardiac function” OR “ Ejection fraction”) Search 4: (“Coronary artery disease” OR “Ischemic heart disease” OR “coronary heart disease”) AND (“Myocardial bridging”) AND (“prognosis”)

Table 1: Search strategy

Inclusion, exclusion criteria

We included studies based on the following inclusion and excluded based on mentioned exclusion criteria.

Inclusion criteria:

1. Must include at least one of the keywords in title/abstract
2. Must be in English
3. In adult population
4. Within last 10 years

Exclusion criteria

1. No mention of either CAD or myocardial bridging
2. Congenital CVD

Two independent authors reviewed selected studies and extracted data on study characteristics, patient demographics, and study quality assessment. We resolved discrepancies with consensus among all authors. The quality of individual included studies was assessed based on the type of study. (Table 2) mentions the quality assessment tools used for each study.

Results

Search results

Outlined in (Figure 1). is our search strategy per PRISMA guidelines. Of 244 PubMed references and 535 Scopus references by initial search, we applied automated filters (Last ten years, human studies only, age over 18 years and English language in PubMed and studies limited to medicine and health profession, in last ten years, in English language and final reports in Scopus) which yielded 304 records for screening. Eight duplicate records were removed. The titles were screened using the inclusion and exclusion criteria described above and included 40 records. We excluded 4 records as full-text articles could not be retrieved. We assessed thirty- six reports for eligibility. We excluded eight records for no mention of CAD or relation of CAD with MB in the text, one as they lacked data on included patient characteristics. The reviewers independently classified the articles as ‘included’ or ‘excluded,’ with discrepancies resolved by consensus. We assessed the quality of each paper using tools per study type, mentioned in Table 2, and studies with low risk of bias and scores more than and equal to 5 were selected. Two studies were excluded due to the high risk of bias. Twenty-five studies were included in the final review.

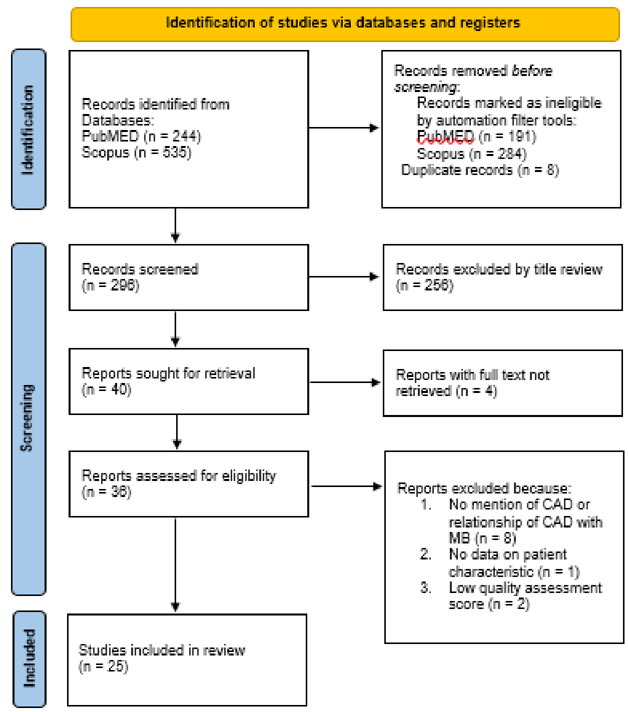

Figure 1: Flow chart for study selection

Study characteristics

Twenty-five studies were reviewed, with most studies being observational (23), followed by case reports (1) and RCT (1). Studies were conducted between the years 2013 to 2023. Table 3 lists individual study details. Most studies reported association between MB of coronary artery disease and/or atherosclerosis (24). One study also reported MB as protective against coronary artery atherosclerosis

Study quality assessment

We assessed all included studies for quality and bias. Tools used for quality assessment were based on the type of study. (Table 2) mentions the respective tools used for each included study. We included studies if they had an overall low risk of bias in assessment or a score of 5 or more in the risk assessment tool.

Author	Year of publication	Type of study	Quality assessment tool	Score
van der Velde et al [3]	2020	Observational	New Castle Ottawa	8
Sara, J. D. S. et al [4]	2020	Observational	New Castle Ottawa	8
Javadzadegan, A. et al [5]	2019	Observational	New Castle Ottawa	6
Monroy-Gonzalez, A. G. et al [6]	2018	Observational	New Castle Ottawa	6
Lee, C et al [7]	2014	Observational	New Castle Ottawa	7
Verhagen, S. N., Rutten et al [8]	2013	Cross sectional	New Castle Ottawa	6
Papp, S. et al [9]	2021	Observational	New Castle Ottawa	6
Nakaura, T. et al [10]	2014	Observational	New Castle Ottawa	7
Jiang, L et al [11]	2018	Observational	New Castle Ottawa	7
Akishima-Fukasawa, Y. et al [12]	2018	Observational	New Castle Ottawa	6
Zhou, F. et al [13]	2015	Observational	New Castle Ottawa	6
Lu, Y. et al [14]	2023	Observational	New Castle Ottawa	8
Tanaka, S. et al [15]	2023		New Castle Ottawa ROB tool	6
Bhogal, S. et al [16]	2023	Case report		6
Saito, K. et al [17]	2022	Observational	New Castle Ottawa	7
Saito, K. et al [18]	2022	Observational	New Castle Ottawa	7
György Bárczi et al [19]	2022	Observational	New Castle Ottawa	6
Çetin, N. et al [20]	2021	Observational	New Castle Ottawa	7
Yu, Y. et al [21]	2021	Observational	New Castle Ottawa	8
McLaughlin, T et al [22]	2021	Clinical trial		Low risk
Matta, A. et al [23]	2021	Observational	New Castle Ottawa	8
Zhao, D. et al [24]	2019	Observational	New Castle Ottawa	5
Rajendran, R. et al [25]	2019	Observational	New Castle Ottawa	7
Nafakhi, H. et al [26]	2019	Observational	New Castle Ottawa	4
Hao, Z. et al [27]	2018	Observational	New Castle Ottawa	6

Table 2: Quality assessment of included studies

Baseline characteristics of patient populations

A total of 56,189 participants were included in the cumulative analysis of all studies. The average age of patients was between 46 to 74 years. About 35 to 80 % of patients were males with MB of coronary artery. No stratification was found per ethnicity or disease severity in patients with MB.

Myocardial bridge characteristics

14 studies reported MB in left anterior descending coronary artery. Diagnosis was made either during coronary angiography or via Computed tomography coronary angiography.

Author	Year of publication	Type of study	No of participants	Purpose	Conclusions
van der Velde et al [3]	2020	Retrospective observational study	248	MB, Calcium score, plaque morphology, presence, and extent of CAD.	MB in HCM is associated with myocardial ischemia. No association with cardiovascular mortality and nonfatal adverse cardiac events.
Sara, J. D. S. et al [4]	2020	Prospective observational study	1469	Prevalence of MB associated with coronary endothelial dysfunction in patient with chest pain and non-obstructing CAD.	Higher frequency of endothelial dysfunction (60%) in patients with MB in LAD.
Javadzadegan, A. et al [5]	2019	Prospective observational study	20	Relationship between Myocardial bridging and endothelial dysfunction.	MB and endothelial dysfunction were associated with increased shear stress in mid LAD – predisposing to non-obstructive CAD angina.
Monroy-Gonzalez, A. G. et al [6]	2018	Retrospective observational study	131	Effect of Myocardial bridging of the left anterior descending coronary artery on myocardial perfusion reserve.	MB of LAD associated with reduced myocardial perfusion reserve.
Lee, C et al [7]	2014	Prospective observational study	551	Impact of myocardial bridging on the long-term clinical outcomes of patients with LAD CAD treated with a drug-eluting stent.	Rate of MACE higher in MB in patients with LAD CAD with DES.
Verhagen, S. N., Rutten et al [8]	2013	Cross sectional	128	Relationship between myocardial bridges and reduced coronary atherosclerosis in patients with angina pectoris.	Patients with stable and unstable angina coronary artery segments covered with MB have lower Angaston calcium score than segments without MB.
Papp, S. et al [9]	2021	Retrospective observational study	100	Effect of Coronary plaque burden of the LAD artery in patients with or without MB.	Coronary plaque burden of LAD in patients with MB has no effect on prognosis.
Nakaura, T. et al [10]	2014	Retrospective observational study	188	To study association between MB and coronary atherosclerosis in the segment proximal to the site of bridging.	Segment of coronary artery proximal to segment with MB is at increased risk of atherosclerosis although the tunneled segment is spared.

Jiang, L et al [11]	2018	Retrospective observational study	6774	To study potential protective effect of MB against severe obstructive atherosclerosis in the whole coronary system.	Rate of severe obstructive CAD requiring PCI/CABG was much lower in patients with MB. MB has some protective role in preventing severe CAD.
Akishima-Fukasawa, Y. et al [12]	2018	Retrospective observational study	150	Assessment of Stenotic Site and Risk Factor for Atherosclerosis in LAD Coronary Artery by MB.	MB enhances left LAD artery atherosclerosis development at a site proximal to MB entrance.
Zhou, F. et al [13]	2019	Retrospective observational study	188	To use machine Learning Using CT-FFR to predict if Proximal Atherosclerotic Plaque Formation is Associated with LAD MB.	FFR in CCTA is a strong predictor for plaque formation in LAD MB.
Lu, Y. et al [14]	2023	Retrospective observational study	2557	Assessment of MB and the peri-coronary fat attenuation index to predict CAD risk.	MB systolic stenosis assessed by coronary CT was independent predictor of atherosclerotic risk.
Tanaka, S. et al [15]	2023	Retrospective observational study	103	To study impact of myocardial bridging on coronary artery plaque formation and long-term mortality after heart transplantation.	MB appears to relate to accelerated proximal intimal growth and reduced long-term survival in heart-transplant recipients.
Bhogal, S. et al [16]	2023	Case report	1	To assess relation between MB associated endothelial dysfunction and ischemia.	Importance of through work up to rule out the microvascular disease.
Saito, K. et al [17]	2023	Retrospective observational study	98	To study of impact of myocardial bridge on lumen changes in acute coronary syndrome.	Serial lumen changes assessed by minimal lumen diameter are not associated with MB in LAD.
Saito, K. et al [18]	2022	Retrospective observational study	116	Influence of MB on atherosclerotic plaque distribution.	MB could be considered as a predictor of lipid content of atherosclerotic plaque when assessed by NIRS-IVUS imaging.

György Bárczi et al [19]	2022	Retrospective observational study	203	Impact of MB on Long-Term mortality.	Morphological parameters of angina-associated, isolated LAD bridges were more severe compared to bridges that were accidentally found.
Çetin, N. et al [20]	2022	Retrospective observational study	155	Comparison of Framingham risk score and atherogenic indices as a predictor of atherosclerosis in patients with MB in LAD artery.	Framingham Risk Score is an easily applicable predictor in clinical practice that indicates the presence of coronary atherosclerosis in patients with MB in LAD.
Yu, Y. et al [21]	2021	Retrospective observational study	498	To study CT FFR for the Diagnosis of MB-Related Ischemia.	Age and Framingham Risk Score associated with MB in LAD CT-FFR systolic reliably excluded MB-related ischemia. MB showing positive CT-FFR results requires further evaluation.
McLaughlin, T et al [22]	2021	Clinical trial	25	Relationship Between Coronary Atheroma, Epicardial Adipose Tissue Inflammation, and Adipocyte Differentiation Across the Human MB.	Adipogenesis was suppressed in the bridge Epicardial adipose tissue, but only in the presence of atherosclerotic plaque.
Matta, A. et al [23]	2021	Retrospective observational study	35813	LAD MB and its association to atherosclerosis.	Epicardial adipose tissue overlying an atheromatous vessel proximal to the MB would be inflamed compared with overlying the MB.

Zhao, D. et al [24]	2021	Retrospective observational study	1718	To study association between MB-related coronary heart disease.	This study shows a negative association between the presence of LAD-MB and development of significant atherosclerotic disease. MB thickness, systolic compression, diastolic compression, and MCA systolic stenosis is independent influencing factors for MB-related CHD. The combination of these factors has potential diagnostic value for MB-related CHD.
Rajendran, R. et al [25]	2019	Prospective observational study	4500	To study prevalence of myocardial bridging on multidetector computed tomography and its relation to coronary plaques.	MB thickness, systolic compression, and diastolic compression were independent risk factors for MB-related CHD. The prevalence and distribution of coronary plaques in LAD were similar in patients with and without MB.
Nafakhi, H. et al [26]	2019	Retrospective observational study	225	To investigate association between MB characteristics with coronary atherosclerotic markers.	Coronary plaques in LAD are similar in patients with and without MB. MB depth and proximal stenosis presence were significantly associated with coronary plaque and stenosis presence.
Hao, Z. et al [27]	2018	Prospective observational study	330	To study the Outcome of PCI for Significant Atherosclerotic Lesions in Segment Proximal to MB at LAD Coronary Artery	DES implantation for significant atherosclerosis stenosis in the segments proximal to MB have higher incidence of MACEs. MB appears to be associated with a higher incidence of stent restenosis after PCI and is a significant factor in the occurrence of MACEs.
Acronyms used: MB: myocardial bridging, CAD: coronary artery disease, HCM: Hypertrophic cardiomyopathy, LAD: left anterior descending, MACE: Major adverse cardiac events, DES: Drug eluting stents, PCI: Percutaneous intervention, CABG: coronary artery bypass grafting, CT-FFR: Computed tomography-Fractional flow reserve, CCTA: Coronary computed tomography angiography, CT: computed tomography, NIRS-IVUS: Near-infrared spectroscopy intravascular ultrasound imaging, CHD: Coronary heart disease.					

Table 3: Characteristics of individual studies included in the systematic review

Discussion

Myocardial bridging (MB) is a congenital anomaly characterized by the tunneled course of a coronary artery through the myocardium [28]. While traditionally considered a benign condition, emerging evidence suggests that MB can have clinical implications, including myocardial ischemia, exercise-related cardiac events, and an association with myocardial infarction [29].

The anatomical hallmark of MB is the segmental encasement of a coronary artery within the myocardium, leading to systolic compression of the tunneled segment during ventricular contraction. This dynamic phenomenon can result in mechanical obstruction of blood flow, leading to myocardial ischemia and related symptoms [30]. The left anterior descending (LAD) artery is the most affected coronary artery, followed by the right coronary artery and the circumflex artery. MB involving multiple coronary arteries is a less common but significant finding, as it may further compromise coronary blood flow and increase the risk of adverse cardiac events [31].

The pathophysiology of MB involves the compression of the coronary artery during systole due to the overlying myocardial muscle. This compression results in impaired blood flow through the affected artery, leading to a variety of clinical manifestations. The degree of compression varies among individuals and can be influenced by factors such as the depth and length of the myocardial bridge [32]. The compression of the coronary artery during systole leads to mechanical stress on the vessel wall and endothelial dysfunction, which may contribute to the development of atherosclerosis within the bridged segment. Sara, J.D.S. et al in their review showed about 60% patient with MB had higher frequency of endothelial dysfunction [4]. In contrast Javadzadegan, A. in their prospective observational study showed MB was associated with endothelial dysfunction had lower shear wall shear in proximal LAD and greater in mid-LAD than patients with MB without endothelial dysfunction [5]. Additionally, the altered hemodynamics can disrupt the normal myocardial oxygen supply-demand balance, potentially leading to myocardial ischemia and related symptoms [33]. Understanding the pathophysiology of MB is crucial for appropriate diagnosis, risk stratification, and management of individuals with this condition. Van der Valde et al in their study show a correlation between pathogenic DNA variant of hypertrophic cardiomyopathy and presence of MB, however no association with worse outcomes [3].

The clinical manifestations of MB vary widely, ranging from an asymptomatic incidental finding to exertional chest pain, dyspnea, palpitations, and in severe cases, myocardial infarction [34]. The mechanisms underlying symptoms in MB are complex and multifactorial. In addition to mechanical compression, endothelial dysfunction, impaired vasodilation, microvascular dysfunction, and abnormal coronary flow dynamics contribute to the development of myocardial ischemia. The severity of symptoms and the extent of ischemia can be influenced by factors such as the length and depth of the bridged segment, the degree of systolic compression, and the presence of concomitant coronary artery disease [35]. Nakaura T., and Akishima, Y. in their respective retrospective studies reported MB as an independent risk factor for coronary atherosclerosis in proximal LAD, whereas Jiang, L. reported MB as a protective factor in preventing severe CAD by reducing rate of severe obstructive CAD requiring PCI/CABG [10-12]. In this context, the prediction of plaque formation in LAD in patients with MB was studies by Zhou, F. by using fractional flow reserve in CCTA [13].

The diagnosis of MB relies on a combination of clinical assessment, electrocardiographic findings, and imaging modalities. Coronary angiography, computed tomography angiography (CTA), and intravascular ultrasound (IVUS), play a crucial role in the identification and characterization of MB. Coronary angiography remains the gold standard for visualizing the dynamic compression of the tunneled segment during systole. CTA provides detailed anatomical information, while IVUS allows for intraluminal imaging and assessment of vessel wall characteristics [36]. Electrocardiographic changes, such as ST-segment depression, T-wave inversion, and arrhythmias, can provide additional clues suggestive of ischemia in the presence of MB.

The management of MB is tailored to individual patients and guided by the severity of symptoms, the extent of ischemia, and associated risk factors. Medical therapy, including the use of beta-blockers, calcium channel blockers, and nitrates, is often the first-line approach for relieving symptoms and improving myocardial perfusion [36]. In cases where medical therapy fails to provide adequate symptom relief or when there is significant myocardial ischemia, interventions such as percutaneous coronary intervention (PCI) or surgical procedures may be considered. PCI with stent placement aims to alleviate the mechanical obstruction and restore normal coronary blood flow. Surgical options, including coronary artery bypass grafting or myotomy, are reserved for refractory cases or complex anatomical presentations.

Data on prognosis of MB on CAD is limited as review of literature is inconclusive. Lee, C. H. in their prospective cohort study report no difference in MI and all cause death between patients with DES to LAD with or without MB, however rate of major cardiovascular events was higher in MB group especially with target lesion revascularization and ischemia driven by it [7].

Our systematic review has some limitations. Foremost, due to lack of consistency in the reported data on association of MB as a protective vs risk factor for atherogenesis in coronary arteries, a conclusion couldn't be deduced. The nature of included studies was limited as most studies were observational, hence limiting objective results however giving scope for more clinical research to be conducted. No stratification based on gender, ethnicity and disease severity was found in the studies reviewed. Such stratification in future studies can allow for more comprehensive data analysis and allow for more focused management strategies and guidelines.

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Conclusion

In conclusion, myocardial bridging represents a unique cardiac anomaly with potential clinical implications. Although often considered a benign variant, it can lead to significant myocardial ischemia and related complications. Early recognition and accurate assessment of MB are crucial for appropriate management decisions. The use of various diagnostic modalities, including advanced imaging techniques, aids in the evaluation of MB severity and assists in determining the most appropriate treatment approach. Further research is needed to better understand the pathophysiology, natural history, and long-term outcomes associated with MB with respect to CAD, which will ultimately guide optimal management strategies for affected individuals.

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