



Spontaneous coronary artery dissection and associated myocardial bridging: Current evidence from cohort study and case reports

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ABSTRACT

Spontaneous coronary artery dissection (SCAD) is a relatively uncommon and under-diagnosed disease characterized by the dissociation of intima and media of coronary artery wall due to an intimal tear or intramural hemorrhage. The exact pathophysiology of SCAD remains elusive and may involve multiple predisposing or precipitating factors including genetic abnormalities, inherited or acquired vasculopathies, hormonal influences, inflammation, intense exercise, emotional stress, and recreational drugs. Accruing reports, including five case reports and one cohort study, have recently addressed the concurrence of SCAD and myocardial bridging (MB), an anatomic variant in which a segment of the epicardial coronary descends and traverses in the myocardium. Among the patients with coexisting MB and SCAD, the left anterior descending artery was the only artery that harbors both pathologies, with SCAD locating either within the tunneled segment or distal to the MB. No other predisposing factors or precipitating stressors for SCAD were noted. It is hypothesized that the predilection for vasospasm, impaired endothelial function, and disturbed coronary flow dynamics associated with MB bridging could collectively contribute to the development of SCAD. Future studies are warranted to explore the mechanistic implications of MB in patients with SCAD.

Background

Spontaneous coronary artery dissection (SCAD) is the non-traumatic, non-iatrogenic dissociation of intima and media of a coronary artery wall caused by an intimal tear or intramural hemorrhage. As more blood accumulates within the intramural space, the true lumen of the dissected coronary artery is compressed, leading to impeded blood flow and myocardial ischemia. Historically, most SCAD cases were detected on the autopsy of young or middle-aged women experiencing sudden death [1]. Recent studies indicate that SCAD is an uncommon condition, with an estimated incidence of 1 to 4% among individuals undergoing angiographic evaluation for acute coronary syndrome [2]. The exact pathophysiology of SCAD remains unclear and has been postulated to involve multiple predisposing or precipitating factors

including genetic abnormalities, inherited or acquired vasculopathies, hormonal influences, inflammation, intense exercise, emotional stress, and recreational drugs [3–5].

Myocardial bridging (MB) occurs when a coronary artery traverses within the myocardium instead of following its routine path through epicardial fat [6]. Previously regarded as a benign congenital anomaly, MB is currently known to be associated with coronary spasm, myocardial ischemia, and even sudden death [7]. Unlike SCAD, MB is relatively common and has been observed in ~25% of the adult population [6]. Both SCAD and MB predominantly involve the left anterior descending (LAD) artery [8–11]. Notably, there is preliminary evidence of concurrence of these two conditions, raising the question as to whether MB could serve as a cause of SCAD. The article delineates the empirical data, biological plausibility, and future perspectives

Abbreviations: ACh, acetylcholine; LAD, left anterior descending artery; MB, myocardial bridging; SCAD, spontaneous coronary artery dissection

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regarding the potential mechanistic role of MB in the development of SCAD.

The hypothesis

It is hypothesized that the predilection for vasospasm, impaired endothelial function, and disturbed coronary flow dynamics associated with myocardial bridging could collectively contribute to the development of spontaneous dissection of the coronary artery.

Empirical data

A systematic search of PubMed, Embase Ovid, and Google Scholar was performed using the following keywords, with the application of wildcard characters to account for variations in spelling and plurals: “spontaneous coronary artery dissection” in combination with “myocardial bridging” OR “coronary bridging”. Original articles were included if a definitive diagnosis of SCAD and MB was reported. Editorials, reviews, letters or commentaries, and animal studies were excluded. A total of seven patients from six articles (five case reports and one cohort study) were identified.

Reported cases with the concurrence of MB and SCAD were summarized in Table 1. The first case was reported in 2008 by Ge et al., in which an otherwise healthy 41-year-old female presented with a substernal chest pain that was relieved by nitrates [12]. She was managed conservatively with dual antiplatelet therapy, low molecular weight heparin, statin, and angiotensin-converting enzyme inhibitor. MB involving the middle-to-distal LAD was evident on coronary angiography, intravascular ultrasound (IVUS), and coronary computed tomography angiography (CCTA). However, coronary dissection was only detected on IVUS, which demonstrated an intimal tear within the tunneled segment. Given the absence of relevant triggers for SCAD, the authors speculated that MB could have played a mechanical role in the pathogenesis of SCAD by an increased predisposition to vasospasm. The second case was a 35-year-old female with unremarkable history who experienced sudden death presumably due to SCAD [13]. On post-mortem examination, the proximal LAD had an intramyocardial course followed by a non-linear course of dissection. It was suggested that MB could have resulted in weakening and dissection of the vessel wall by applying mechanical stress during systolic contraction. Another case was a 19-year-old male reported by Chaurasia et al., which had an MB followed by SCAD in the middle LAD [14]. In 2014, Aksakal et al. described a case of SCAD lesions in both the LAD and left circumflex artery, and MB was found to coexist with the dissected LAD segment [15]. In 2016, Wu et al. reported a 33-year-old post-partum female without significant past history who had an extensive SCAD in the LAD distal to the MB [16]. It was speculated that vessel wall stress associated with MB could have caused intimal injury and subsequent dissection. Finally, according to a retrospective assessment of CCTA images from an acute SCAD cohort, two out of 14 patients were found to have concurrent MB [17]. In summary, among the seven cases with coexisting MB and SCAD, the LAD was the only artery reported to harbor both pathologies, with SCAD occurring either within the tunneled segment or distal to the MB. No other predisposing factors or precipitating stressors for SCAD were noted in these cases.

Biological plausibility

Several possible mechanisms may be involved in the causal relationship between MB and SCAD. The first theory focuses on vasospasm in the bridged artery, which was initially demonstrated by Grover et al. and confirmed in subsequent studies [18–22]. Specifically, in the setting of MB, systolic kinking of the coronary vessel may result in injury to the intima and endothelium, which in turn produces vasospasm [20,23,24]. Ge et al. linked this phenomenon to SCAD by proposing that the vasospasm in the tunneled artery could increase its susceptibility to

dissection [12]. This mechanism is supported by the simultaneous occurrence of vasospasm and SCAD [25,26]. Upon further exploration, Saito et al. demonstrated that the morphological severity of MB, as evaluated by the total length of the bridge and the degree of systolic compression, was positively correlated to spasm [27].

Another hypothesis posits that endothelial dysfunction associated with MB may also play a role in the pathogenesis of SCAD. Impaired response to vasoactive agents such as acetylcholine (ACh), nitric oxide, and endothelin-1 has been observed in the setting of MB [28]. Although commonly referred to as a vasodilator, ACh can cause paradoxical vasoconstriction of atherosclerotic coronary arteries in the presence of a dysfunctional endothelium [29]. Several studies have also demonstrated ACh-mediated vasoconstriction in the bridged segment [30–32]. Furthermore, evidence suggests ACh may result in vasoconstriction even in sites remote to the bridge (e.g., the brachial artery) [33]. Along with attenuated response to nitric oxide and endothelin-1, two major modulators of coronary diameter and flow, one can suspect ACh-mediated vasoconstriction to play a vital role in the vasospasm that leads to SCAD. Masuda and colleagues further strengthened this theory when they discovered that the endothelial response to these agents was reduced in the bridged artery compared with its proximal and distal segments [34]. Considering so, any vasoconstriction in the bridged area disproportionate to its proximal and distal segments could theoretically lead to vasospasm and dissection of the bridged coronary.

The third postulated mechanism involves disrupted coronary flow dynamics in MB. As suggested by Herrmann and colleagues, flow disturbance caused by the pressure gradient between the bridged and non-bridged segment may lead to a state of chronic coronary pressure overload [32,35]. Chronic coronary pressure overload has been related to alterations in the endothelium including atherogenesis and endothelial disruption [36]. These effects may be more pronounced in deep myocardial bridging and tachycardia. Furthermore, tachycardia could also result in direct intimal trauma to the tunneled vessel by the bridging fibers, which eventually leads to coronary dissection.

Consequences of the hypothesis and discussion

Identification of coexisting MB in SCAD patients may influence the treatment decision and inform the prognostic impact. Recognizing MB as a cause for SCAD leads to a reasonable assumption that treating the MB can protect against the development of SCAD. The management of MB is directed toward preventing the events that could potentially lead to ischemia or spasm. Medical therapy includes beta-blockers as first-line treatment and calcium channel blockers. Beta-blockers reduce cardiac sympathetic drive, especially in response to stress, as well as reducing heart rate, contractility, and the systolic pressure on the tunneled artery [37]. Of note, beta-blocker usage has also been associated with a lower recurrence among SCAD patients [38]. On the other hand, vasodilator such as nitroglycerin should be avoided, as it may exacerbate the disturbed flow dynamics by causing tachycardia, intensified systolic compression of the tunneled artery, and preferential dilatation of the segment proximal to the MB [39]. Other diseases have also been implicated as a potential cause of SCAD, such as fibromuscular dysplasia and takotsubo syndrome [40]. It remains unclear whether the concurrence of SCAD and these conditions would adversely impact the short- and long-term outcome.

Since the release of Position Paper from the European Society of Cardiology and Scientific Statement from the American Heart Association [41,42], there has been an increased awareness of SCAD among patient support groups, healthcare providers, and research organizations. On the contrary, MB has received relatively little attention from major cardiovascular societies. Future research efforts are required to address the following gaps in knowledge. First, current literature concerning the coexistence of MB and SCAD is limited to retrospective data gleaned from five case reports and one small cohort study. Analysis of prospective registries and epidemiological studies

Table 1
Summary of cases demonstrating the association between MB and SCAD.

Year	Author	Age	Sex	Past history	Clinical presentation	Imaging findings		Autopsy findings
						Coronary angiography	Intracoronary imaging	
2008	Ge (12)	41	F	No history of chest pain, cardiac risk factor, episode of connective tissue disease, drug abuse, or recurrent trauma	Squeezing substernal chest pain lasting for 3 h. ECG showed ST-elevation in leads V2 to V5. CK-MB and troponin T were increased.	40–60% diffuse narrowing in the middle and distal LAD and a 50% systolic compression at the proximal part of the lesion segment. RCA and Cx were normal.	IVUS: (1) intramural hematoma in the distal LAD; (2) echolucent zone on the side of the artery with the lumen cross-sectional area variation of 42%, suggesting the presence of MB; (3) an intimal tear within the bridge segment; (4) no evidence of atherosclerosis	Mild narrowing of the LAD with no evidence of SCAD
2012	De-Giorgio (13)	35	F	Unremarkable	Sudden death	–	–	Gross examination: The LAD showed a non-linear course of dissection. There was also an intramyocardial course proximal to the dissection. Atherosclerotic plaques were found in the LAD proximal to the MB. Histologic examination: There was bleeding within the coronary artery wall with massive infiltration of the adventitia.
2013	Chauracia (14)	19	M	Mitral stenosis	NYHA class II-III dyspnea without angina	A linear translucency in the LAD following MB. Other vessels were normal.	–	–
2014	Aksakal (15)	70	M	Smoking 10 years ago; no history of cardiac disease	Chest pain lasted for one hour. ECG showed ST depression in leads VI to V3.	Two SCAD lesions were identified: One in the Cx followed by a total occlusion, and the other in the mid LAD complicated by MB.	–	–
2016	Wu (16)	33	F	No history of diabetes mellitus, hypertension, or dyslipidemia, alcohol or drug abuse, or smoking	Exertional chest pain. ECG showed anterior wall MI.	Severe compromise of blood flow in the LAD	OCT: extensive dissection in the LAD distal to the MB. The RCA and the Cx were normal.	–
2018	Tweet (17)	38	–	–	Chest pain climbing stairs, first troponin negative then increased, NSTEMI	–	–	Abrupt luminal stenosis with occlusion at the bridging segment in the LAD and epicardial fat stranding. Abrupt luminal stenosis; LAD bridging not adjacent to SCAD.
2018	Tweet (17)	33	–	–	Nocturnal chest pain, postpartum, ECG changes	–	–	–

Abbreviations: CK-MB, creatine kinase-muscle/brain; CCTA, coronary computed tomography angiography; Cx, left circumflex artery; ECG, electrocardiography; IVUS, intravascular ultrasound; LAD, left anterior descending artery; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; NYHA, New York Heart Association Functional Classification; OCT, optical coherence tomography; RCA, right coronary artery; SCAD, spontaneous coronary artery dissection.

may provide insights into the incidence, demographic characteristics, anatomical features, and prognosis. Second, SCAD may be an angiographic phenotype with a multifactorial pathogenesis. More studies are required to elucidate the mechanistic relationship between MB and SCAD. Last, although beta-blockers may relieve ischemic symptoms and reduce sympathetic tone, the clinical benefit has not been formally examined in patients with MB and SCAD. Future research is needed to devise the optimal treatment strategy for this unique population.

Declaration of Competing Interest

The work is not funded and the authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2019.05.012>.

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