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CASE REPORT

CLINICAL CASE

Myocardial Bridging as a Trigger in Angina With No Obstructive Coronary Artery Disease

Marcel A.M. Beijk, MD, PhD,[a] Janneke Woudstra, MD,[a] A. Suzanne Vink, MD, PhD,[a] Nick R. Bijsterveld, MD, PhD,[a] Robert A.F. de Lind van Wijngaarden, MD, PhD,[b,c] Robert J.M. Klautz, MD, PhD[b,c]

ABSTRACT

We present 2 patients with angina with no obstructive coronary artery disease and concomitant myocardial bridging. Despite maximal tolerated pharmacotherapy, symptoms remained. Invasive anatomical and hemodynamic assessment identified myocardial bridging as a contributing cause of angina. Following heart team discussion, both patients underwent successful coronary artery unroofing of the left anterior descending artery. (J Am Coll Cardiol Case Rep 2024;29:102382) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Coronary vasomotor disorders (CVDys) are a well-recognized cause of angina in patients with no obstructive coronary artery disease (ANOCA). Intracoronary function testing (ICFT) can adequately diagnose CVDys with abnormal vasoconstriction, abnormal vasodilatation, or a combination of both.[1] Current guidelines emphasize ICFT should be applied routinely in ANOCA patients.

Myocardial bridging (MB) is an underdiagnosed cause of ANOCA and associated with a poor prognosis. The prevalence of MB in ANOCA patients varies between 30% and 60% depending on the type of imaging performed.[2] Coronary computed tomography angiography (CTA) and intravascular ultrasound (IVUS) have a greater accuracy to detect MB than coronary angiography (CAG).[2] The hemodynamic significance of MB should be determined by measuring the diastolic flow gradient during dobutamine stress.[3] Previous studies demonstrated that

LEARNING OBJECTIVES

- To recognize that MB is an underdiagnosed cause of ANOCA with a prevalence up to 60%, depending on the type of imaging test performed.
- To evaluate the hemodynamic significance of the MB in patients with coronary vasomotor disorders, a dobutamine stress diastolic FFR should be performed with a low threshold.
- To be able to understand that if symptoms remain despite optimal pharmacotherapy, revascularization should be considered wherein preprocedural anatomic planning with coronary CTA or IVUS is crucial to guide revascularization strategy.
- To manage very deep (≥5 mm) or long (≥25 mm) MBs, surgical unroofing or coronary artery bypass grafting may be indicated to relieve symptoms.

From the [a]Amsterdam UMC, Heart Center, Department of Cardiology, Amsterdam Cardiovascular Sciences, Amsterdam, the Netherlands; [b]Department of Cardiothoracic Surgery, Amsterdam University Medical Center, Amsterdam, the Netherlands; and the [c]Department of Cardiothoracic Surgery, Leiden University Medical Center, Leiden, the Netherlands.

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ABBREVIATIONS AND ACRONYMS

ANOCA = angina with no obstructive coronary artery disease

CAG = coronary angiography

CTA = computed tomography angiography

ECG = electrocardiogram

ICFT = intracoronary function testing

IVUS = intravascular ultrasound

MB = myocardial bridging

patients with MB undergoing ICFT show epicardial spasm in up to 70% to 80%.[4] We present 2 patients with CVDys and refractory symptoms despite optimal pharmacotherapy with concomitant hemodynamically significant MB.

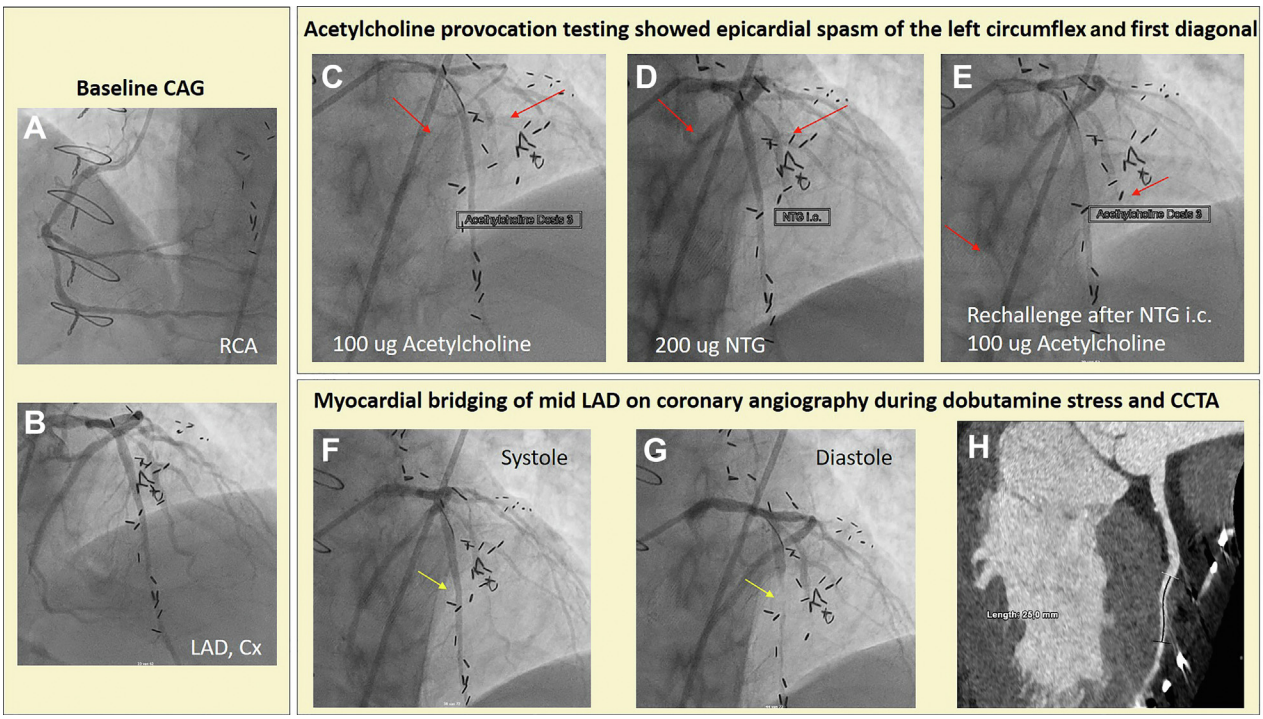
PATIENT 1

A 59-year-old man with known hypertension, non-ST-segment elevation myocardial infarction, and coronary artery bypass grafting 1 year prior with a left internal mammary artery (LIMA) to diagonal (D) and left anterior descending (LAD) and radial artery from aorta to circumflex (Cx), was referred to our outpatient clinic because of refractory angina during exercise and at night. Cardiac magnetic resonance (CMR) revealed ischemia in the LAD territory. CAG showed a long segment of MB mid-LAD, a significant stenosis of the first D and Cx, and LIMA-D-LAD was nonfunctional because of kinking. The radial-Cx had significant ostial stenosis. Percutaneous coronary intervention was performed of first D and Cx (**Figures 1A and 1B**). After 4 weeks, the patient reported relieve of exercise-related angina but remained symptomatic at night.

Under suspicion of CVDys, ICFT was performed. Step-wise injection of acetylcholine (Ach) up to 100 μg provoked recognizable angina, prominent ST-segment depression in leads I and aVL and ST-segment elevation in all other leads of the ECG, and >90% vasospasm of first D and Cx (**Figure 1C**, Video 1). After intracoronary nitroglycerine administration, symptoms resolved, and ECG changes and vasospasm normalized (**Figure 1D**). Ach-rechallenge with 100 μg showed recurrence of vasospasm (**Figure 1E**). Pharmacotherapy for vasospasm was initiated but hampered because of intolerance to calcium antagonists, long-acting nitrates, alpha-blockers, and ivabradine. Treatment with molsidomine and macitentan allowed the patient to return to his daily activities.

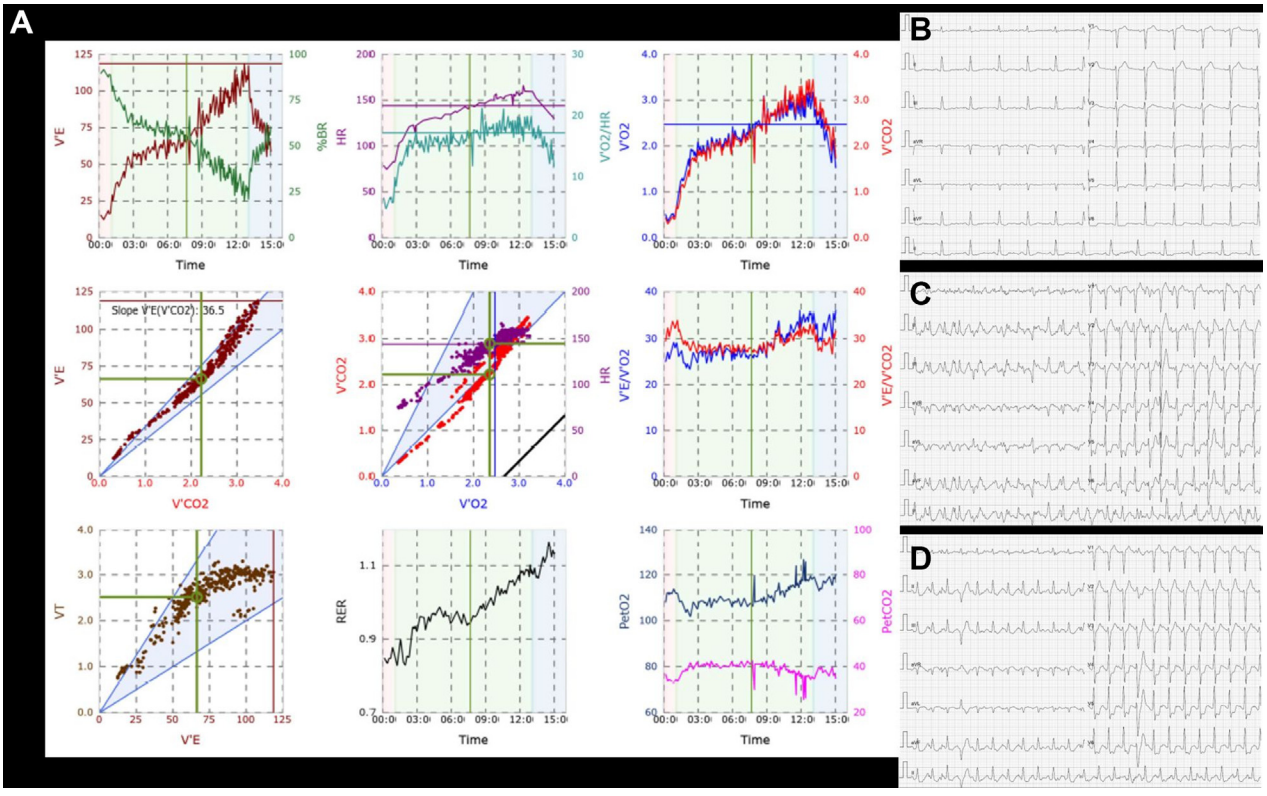
After 3 years, progression of angina occurred and CAG showed no obstructive coronary artery disease.

FIGURE 1 CAG and Coronary CTA of Case 1



Baseline coronary angiograms (CAGs) of right coronary artery (RCA) (A) and left coronary artery (LCA) (B). Intracoronary function testing showing epicardial spasm of circumflex (Cx) and first diagonal (red arrows) (C), relaxation of LCA after intracoronary nitroglycerine (D), and recurrence of spasm during acetylcholine rechallenge (red arrows) (E). Dobutamine stress angiography during systole (F) and diastole (G) showing compressed mid-LAD (yellow arrows), and coronary computed tomography angiography (CTA) (H).

FIGURE 2 **Cardiopulmonary Exercise Testing of Case 2**



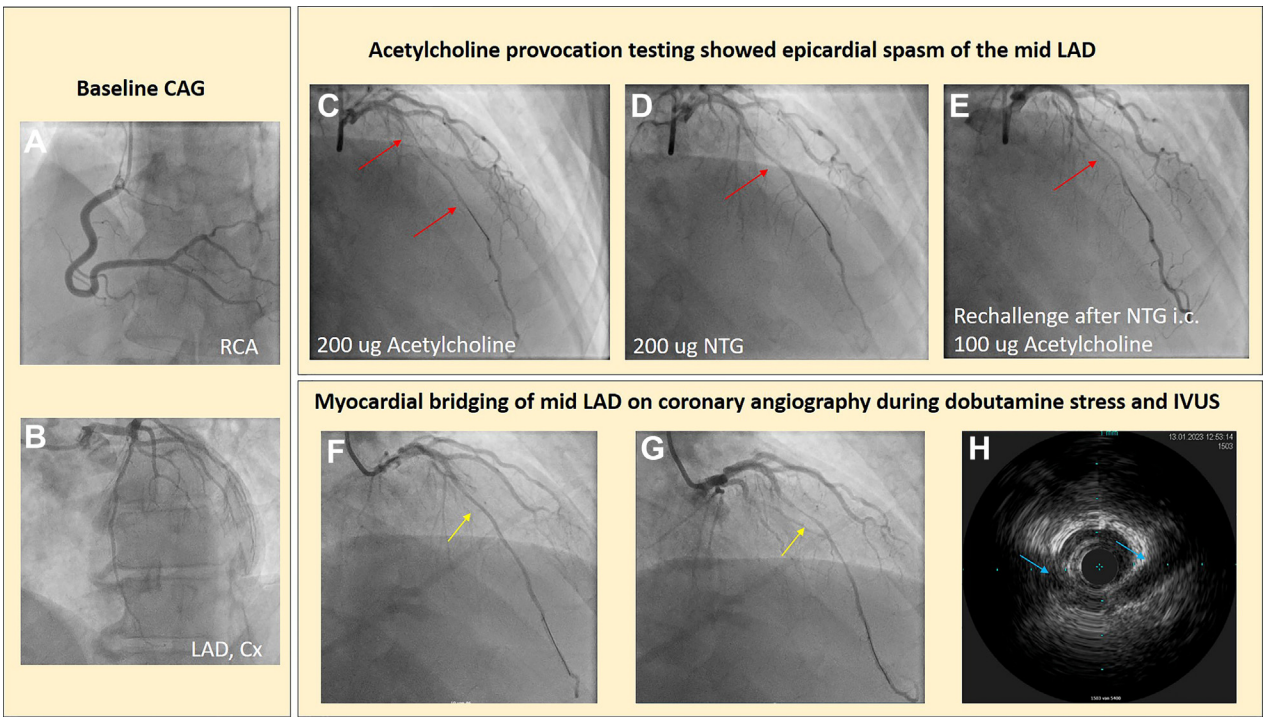
9-panel plot of cardiopulmonary exercise testing (A). Electrocardiograms at the start of the cardiopulmonary exercise testing (B), at maximal exercise (C), and in recovery phase (D).

IVUS revealed 50 mm MB of mid-LAD. Hemodynamic measurements with Verrata-Volcano pressure-wire (Philips) were performed distal to the MB at rest and during peak dobutamine stress testing. Dobutamine given intravenously in increments of 10 μg/kg/min every 3 minutes up to 30 μg/kg/min. At a heart rate of 131 beats/min, the patient had recognizable angina with an instantaneous wave-free ratio (iFR) of 0.64 (**Figures 1F and 1G**, Video 2). The patient was discussed in the heart team and accepted for surgical unroofing. Preoperative coronary CTA revealed MB of 2.5 cm in length with maximal 3.5 mm depth of the LAD (**Figure 1H**). Surgery was performed via (redo) median sternotomy and with cardiopulmonary bypass. Warm blood cardioplegia was applied but was limited to 20-minute intervals. A 5-cm length of mid-LAD, just proximal to the LIMA anastomosis, was successfully unroofed from the cardiac muscle. Postoperative recovery was uneventful, and the patient was discharged without any antianginal medication. After 10 months, the patient's symptoms improved significantly with only 1 mild attack of angina for which molsidomine was restarted.

PATIENT 2

A 56-year-old type 1 diabetic man was referred to our outpatient clinic because of exercise-induced angina. Cardiopulmonary exercise testing revealed normal VO_2max at maximal heart rate of 160 beats/min, maximum blood pressure of 180/55 mm Hg, and recognizable symptoms. His ECG showed ST-segment depression of >2 mm in the lateral leads (**Figure 2**). CMR showed no evidence of ischemia; however, because of persistent symptoms, CAG was performed showing no obstructive coronary artery disease (**Figures 3A and 3B**) with MB of mid-LAD. He underwent ICFT to evaluate the presence CVDys. Injection of 200 μg Ach provoked recognizable angina and 50% to 90% spasm of mid-LAD at the site of MB (**Figure 3C**, Video 3). The ECG did not change during Ach provocation. After intracoronary nitroglycerine administration, relief of symptoms occurred and

FIGURE 3 CAG and IVUS of Case 2



Baseline angiograms of RCA (A) and LCA (B). Intracoronary function testing showing epicardial spasm of mid-LAD (red arrows (C), relaxation of LAD after intracoronary nitroglycerin (NTG) (D), and less spasm during acetylcholine rechallenge (red arrow) (E). Dobutamine stress angiography during systole (F) and diastole (G) showing compressed mid-LAD (yellow arrow), intravascular ultrasound (IVUS) showing typical "halo-sign" (blue arrows) (H). Abbreviations as in **Figure 1**.

spasm normalized (**Figure 3D**). Ach-rechallenge with 200 μg showed less spasm (**Figure 3E**). Treatment for vasospasm was initiated with a calcium antagonist.

In the 2 years following, the symptoms worsened despite maximal tolerated pharmacotherapy. Treatment with ivabradine or nebivolol for MB did not improve symptoms. Hemodynamic measurements of MB during 40 μg/kg/min dobutamine, at a heart rate of 140 beats/min, induced recognizable angina and an iFR of 0.63 (**Figures 3F and 3G**, Video 4). IVUS revealed a 44-mm MB of mid-LAD (**Figure 3H**). The patient was discussed in the heart team and accepted for surgical unroofing. A total length of 6 cm MB of mid-LAD was successfully unroofed from the cardiac muscle. Postoperative recovery was uneventful, and he was discharged without any antianginal medication. At 12-month follow-up, he was asymptomatic.

DISCUSSION

We present 2 ANOCA patients with CVDys who remained symptomatic despite optimal pharmacotherapy. Hemodynamic evaluation identified MB as an important contributing cause of angina, and after surgical unroofing, the patients improved significantly.

MB is a dynamic stenosis caused by an abnormal intramyocardial course of a segment of an epicardial coronary artery. Although the coronary artery fills during diastole and compression from MB occurs in systole, studies demonstrated a delayed early diastolic artery relaxation leading to a decrease of vessel luminal diameter in diastole.[5-7] MB is mostly considered benign, but in particular, bridging of proximal or mid-LAD is associated with vasospastic angina.[4]

In symptomatic patients with CVDys and MB, it is essential to perform a detailed noninvasive and invasive assessment. ICFT evaluates the coronary vasomotor response in reaction to intracoronary administered pharmacological stimuli, ie, Ach (endothelial-dependent vasodilator), and will evaluate CVDys that result in vasoconstriction. In the assessment of MB, multimodality imaging is recommended. Coronary CTA has an accurate detection of the length of MB and course of the artery, ie, normal (within the epicardial fat), superficial intramyocardial (<2 mm), deep intramyocardial (≥2 mm), or very deep

(≥5 mm). CMR, myocardial perfusion imaging, and stress echocardiography may identify reversible ischemia in the territory of MB. Evaluation of MB with CAG is limited to the typical "milking" effect, which is only present in approximately 5% of patients, and the degree of compression does not correlate with hemodynamic significance.[2] IVUS allows measurements of the length of MB, thickness of the myocardial band over the artery (typical "half-moon" or halo-sign), vessel wall morphology, vessel lumen diameter, and the percentage of systolic compression (100 × [diastolic vessel area − systolic vessel area]/diastolic vessel area).[8] Optimal coherence tomography is hampered by the penetration depth.

Hemodynamic significance of MB should be assessed using intracoronary pressure wire techniques with measurement distal to the bridge. Due to the dynamic properties of the obstruction related to MB, diastolic fractional flow reserve (FFR) during dobutamine stress is a more sensitive modality for functional assessment than conventional FFR.[3] Dobutamine stress diastolic FFR ≤0.76 is considered hemodynamically significant. Although not validated, nonhyperemic pressure ratios such as iFR or resting full-cycle ratio are appropriate alternatives.

There are no formal European or U.S. guidelines for the management of symptomatic MB and treatment may be challenging, especially in patients with concomitant CVDys. Pharmacotherapy can be initiated with beta-blockers (nebivolol), calcium antagonist when beta-blockers are contraindicated (ie, epicardial vasospasm), or ivabradine in maximal tolerated doses. Vasodilating agents should be used with caution in MB because it may worsen systolic narrowing of the artery leading to worsening of symptoms. If symptoms remain despite optimal pharmacotherapy, revascularization should be considered. Preprocedural anatomic planning with coronary CTA or IVUS is crucial to guide revascularization strategy. Surgical unroofing or coronary artery bypass grafting is indicated in very deep (≥5 mm) or long MBs (≥25 mm). Percutaneous coronary intervention, using high radial-strength drug-eluting stents, may be considered in superficial and shorter-length MBs because of the risk of in-stent restenosis and stent fracture.

In conclusion, patients diagnosed with CVDys and concomitant MB who remain symptomatic despite pharmacotherapy should be evaluated for the hemodynamic significance of MB and receive appropriate treatment accordingly.

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ADDRESS FOR CORRESPONDENCE: Dr Marcel A.M. Beijk, Amsterdam University Medical Center, location AMC, Meibergdreef 9, 1105 AZ, Amsterdam, the Netherlands. E-mail: m.a.beijk@amsterdamumc.nl.

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APPENDIX For supplemental videos, please see the online version of this paper.