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CASE REPORT
Adult congenital heart disease

Going under the bridge: unmasking ischaemia and endothelial dysfunction of myocardial bridging: a case report

Sukhdeep Bhogal, Ron Waksman *, and Hayder Hashim

Section of Interventional Cardiology, MedStar Washington Hospital Center, 110 Irving St. NW, Suite 4B1, Washington, DC 20010, USA

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Background Physiological assessment of myocardial bridging prevents unnecessary interventions. Non-invasive workup or visual coronary artery compression may underestimate the underlying ischaemia associated with myocardial bridging in symptomatic patients.

Case summary A 74-year-old male presented to the outpatient clinic with chest pain and shortness of breath on exertion. He underwent coronary artery calcium scan showing an elevated calcium score of 404. On follow-up, he endorsed progressive worsening of symptoms with chest pain and decreased exercise tolerance. He was then referred for coronary angiography that revealed mid-left anterior descending myocardial bridging with initial normal resting full-cycle ratio of 0.92. Further workup after ruling out coronary microvascular disease demonstrated abnormal hyperaemic full-cycle ratio of 0.80 with a diffuse rise across the myocardial bridging segment on pullback. Our patient also had increased spastic response to hyperaemia on angiography, supporting the presence of underlying endothelial dysfunction and ischaemia, likely contributing to his exertional symptomology. The patient was started on beta-blocker therapy with improvement in symptoms and resolution of chest pain on follow-up.

Conclusion Our case highlights the importance of thorough workup of myocardial bridging in symptomatic patients to better understand the underlying physiology and endothelial function after ruling out microvascular disease and consideration of hyperaemic testing if symptoms are suggestive of ischaemia.

Keywords Myocardial bridging • Resting full-cycle ratio • Fractional flow reserve • Case report • Endothelial dysfunction • Myocardial ischaemia

ESC Curriculum 3.1 Coronary artery disease • 3.4 Coronary angiography • 3.3 Chronic coronary syndrome

Learning points

- Non-invasive workup or visual coronary artery compression may underestimate the underlying ischaemia associated with myocardial bridging.
- Thorough workup, including assessment of physiological indices across myocardial bridging, can better delineate the underlying mechanism contributing to symptomology.

* Corresponding author. Tel: +1 202 877 2812, Fax: +1 202 877 2715, Email: ron.waksman@medstar.net
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Introduction

Myocardial bridging is a congenital anomaly that occurs when a segment of epicardial coronary artery takes an intramuscular course and is characterized by systolic compression of the tunnelled artery under the muscular bridge. Physiological assessment across the myocardial bridging is important to prevent unnecessary interventions.[1] Non-invasive workup or visual coronary artery compression may underestimate the underlying ischaemia associated with myocardial bridging in symptomatic patients. We herein present a case of myocardial bridging that did not appear to have significant systolic compression on coronary angiography and had a normal resting full-cycle ratio (RFR); however, further workup revealed significant ischaemia and epicardial endothelial dysfunction following intravenous (IV) adenosine administration.

Timeline

9th September 2021	Patient presented to the outpatient clinic with chest pain and shortness of breath.
27th September 2021	Coronary artery calcium scan was performed.
15th December 2021	Cardiology follow-up visit and referred for coronary angiography.
20th December 2021	Coronary angiography was performed.
31st January 2022	Follow-up visit, patient reported improvement in symptoms and the dose of the selected beta-blocker was escalated.

Case presentation

History of presentation

A 74-year-old male presented to the outpatient clinic after experiencing chest pain and shortness of breath on exertion for the previous 2–3 months. The patient had an unremarkable clinical examination, with blood pressure of 121/63 mmHg and heart rate of 80 b.p.m. Baseline electrocardiogram showed normal sinus rhythm. He underwent coronary artery calcium scoring via computed tomography scan and was found to be elevated at 404 (266 in the left anterior descending [LAD] artery and 138 in the left circumflex artery [LCx]). Transthoracic echocardiogram showed normal ejection fraction and no significant valvular abnormality. On follow-up, he reported progression of his symptoms with decreased exercise tolerance.

Past medical history

The patient had past medical history significant of hypertension, hyperlipidaemia, and obstructive sleep apnoea.

Differential diagnosis

In our case, the key differential diagnoses were epicardial coronary artery disease, microvascular disease, and myocardial bridging.

Investigation

Given his risk factors and continuing symptoms, our patient was scheduled for coronary angiography, which revealed mild proximal LAD disease with mid LAD myocardial bridging (see Supplementary material online, *Video S1*). No significant disease was noted in the LCx or right coronary artery. Right heart catheterization was performed given shortness of breath and due to elevated right ventricular systolic pressure of 45 mmHg on echocardiogram. Catheterization showed normal cardiac output of 6.0 L/min with normal haemodynamics, including pulmonary capillary wedge pressure of 11 mmHg and mean pulmonary artery pressure of 20 mmHg. To better delineate the underlying pathophysiology, RFR of the mid-LAD was performed and noted to be normal at 0.92 (*Figure 1*). Further, we performed a thermodilution coronary flow reserve (CFR) measurement at rest and at maximal hyperaemia using Pressure Guidewire X (Abbott) and the Coroventis CoroFlow System (Abbott) with IV adenosine at a standard dose of 140 mcg/kg/min. This revealed a normal CFR value of 2.6 and a normal index of microcirculatory resistance value of 14 (*Figure 2*), ruling out microvascular disease and suggesting epicardial phenomenon for symptomology. Fractional flow reserve (FFR) at maximal hyperaemia was 0.69. As diastolic physiological indices are better parameters of physiological evaluation in myocardial bridging, we repeated full-cycle ratio following IV adenosine administration and found it to be abnormal at 0.80 with a diffuse rise across the myocardial bridging segment on pullback (*Figure 3*). This allowed us to better delineate the underlying mechanism of myocardial bridging contributing to exertional symptomology.

Management

Our patient was treated with targeted medical therapy using a beta-blocker. Additionally, cardiac rehabilitation was pursued. Invasive surgical unroofing was preserved for failure of initial medical management.

Follow-up

On follow-up at 40 days, our patient reported improvement in exertional symptoms, with resolution of chest pain, and the dose of the selected beta-blocker was escalated (metoprolol, 25 mg daily to 50 mg daily).

Discussion

First recognized by Reyman in 1737 during an autopsy, myocardial bridging is described as an intramuscular course of an epicardial artery.[2] It is a congenital anomaly most commonly present in the middle segment of the LAD and is characterized by systolic compression of the tunnelled artery under the muscular bridge. Based on autopsy studies, the prevalence ranges from 5% to 86%.[2] Although myocardial bridging is clinically silent in the majority of cases, it can present with diverse symptomology including ischaemic symptoms, acute coronary syndrome, malignant arrhythmias, and even sudden cardiac death.

The physiological measurements across the myocardial bridging are of paramount importance for several reasons: (1) they simulate dynamic obstruction contributing to ischaemic symptoms; (2) they evaluate fixed obstruction associated with the bridge; and (3) they unmask underlying endothelial dysfunction.[1] Therefore, physiological assessments during diastole, including diastolic FFR (dFFR) and instantaneous wave-free ratio (iFR), have been found to provide better haemodynamic assessment than the mean FFR.[3] In similar regards, RFR is a novel non-hyperaemic-free resting measure of maximal relative pressure difference (P_d/P_a) of the lowest resting diastolic pressure (P_d) to aortic pressure (P_a), providing unbiased physiological evaluation of the severity of coronary artery stenosis in the cardiac cycle irrespective of systole or diastole.[4] RFR is diagnostically equivalent to iFR and overcomes the limitations of iFR pertaining to the wave-free period.[4,5]

Coronary artery stenosis resting waveform typically exhibits 'diastolic dipping' of P_d in late diastole.[6] The present case demonstrated an initial normal RFR waveform (*Figure 1*); however, induction of hyperaemia led to an early diastolic P_d drop and further loss of parallel down sloping

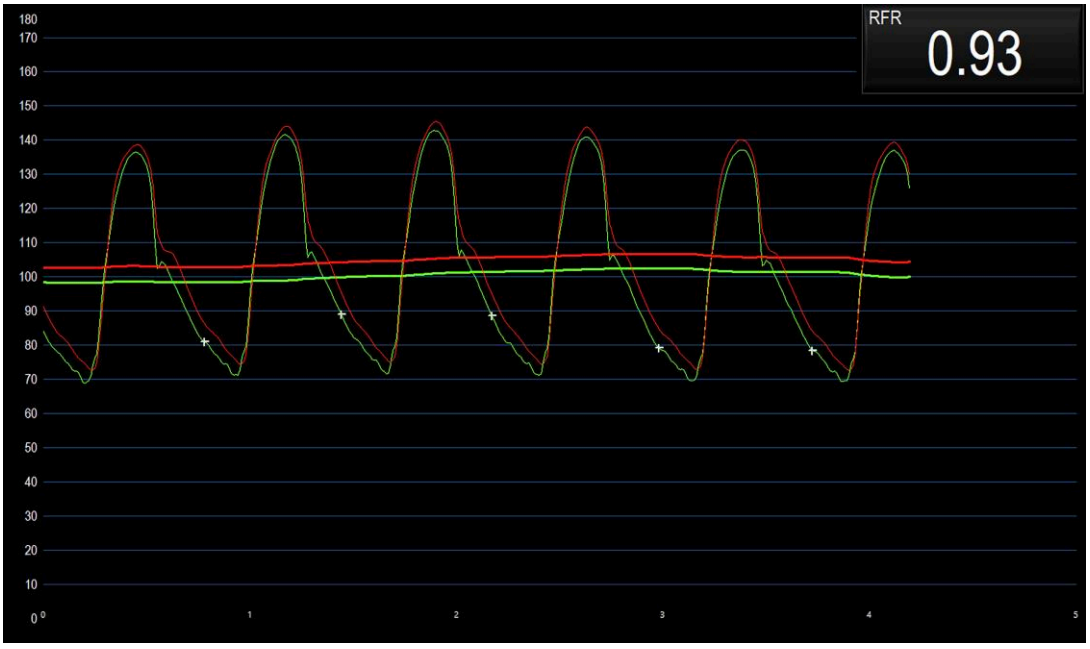

Figure 1 Normal resting full-cycle ratio of mid left anterior descending artery myocardial bridging.

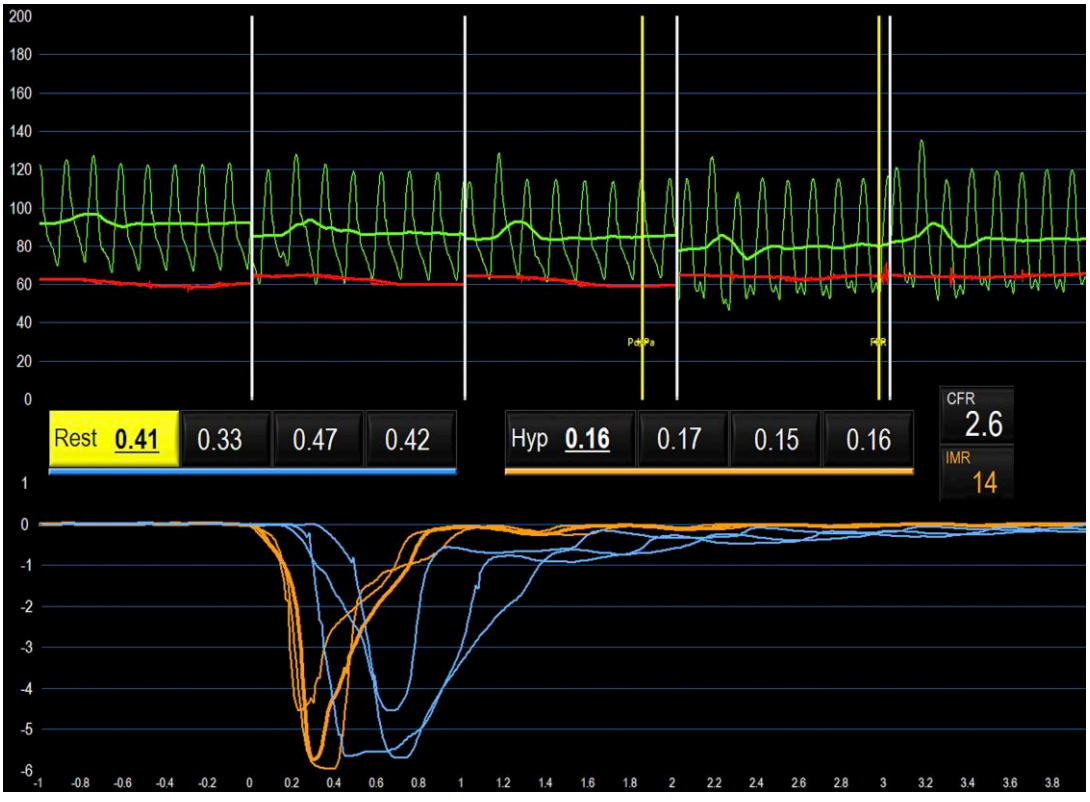

Figure 2 Thermodilution coronary flow reserve measurement at rest and at maximal hyperaemia following adenosine administration showing normal coronary flow reserve and index of microcirculatory reserve values.

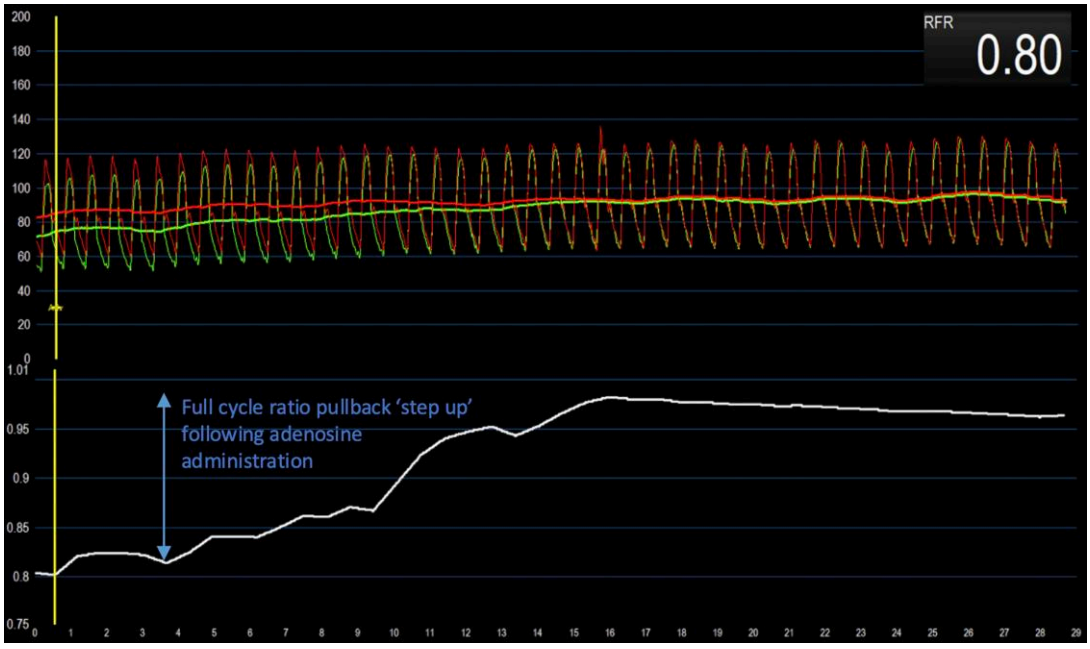

Figure 3 Full-cycle ratio following adenosine administration with a diffuse rise across the myocardial bridging segment on pullback.

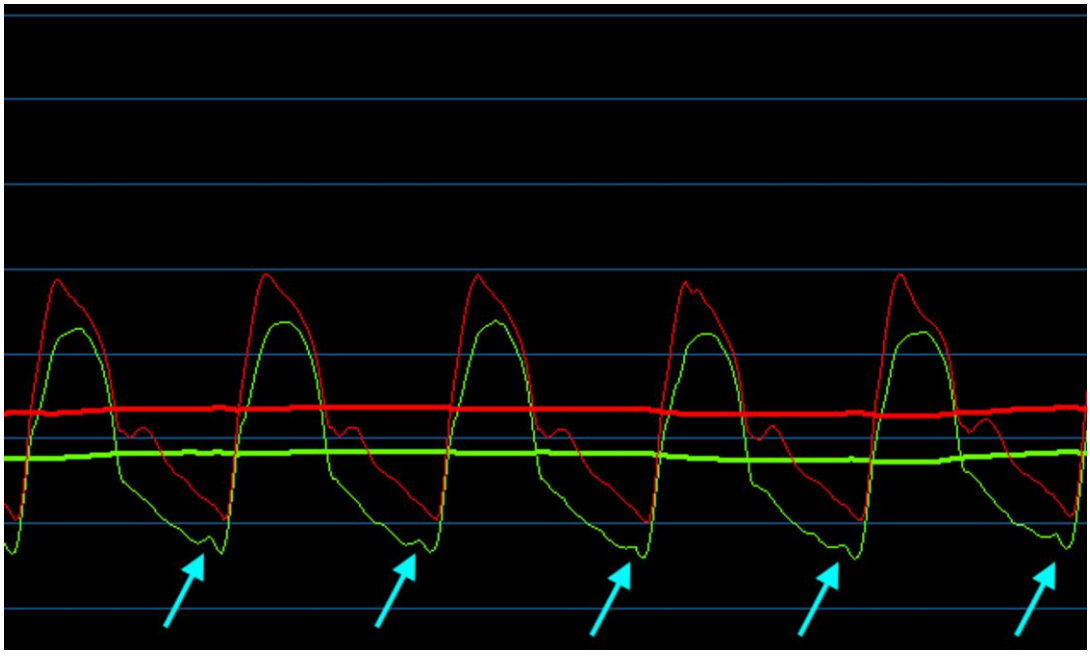

Figure 4 Full-cycle ratio following adenosine administration resulting in loss of parallel down sloping in the entire diastole in comparison to aortic waveform (P_a) and late diastolic dipping of P_d (arrows).

in the entire diastole in comparison to the aortic waveform (P_a) (*Figure 4*), simulating severe coronary stenosis (see Supplementary material online, *Video S2*). Traditionally, myocardial bridging is considered to have limited or no flow in the systole, followed by augmentation of coronary flow in the early stages of diastole and plateauing in mid-late diastole.[7] Due to the dynamic nature and intra-individual variability of myocardial bridging, the pattern of diastolic dipping can also vary, ranging from an early diastolic dip[8] to a late one, as in the present case (*Figure 4*).

Adenosine binds to its A2a on the surface of vascular smooth muscle, activating adenylate cyclase, resulting in cyclic adenosine 5-monophosphate (cAMP) accumulation and activation of protein kinase A.[9] The latter results in hyperpolarization of vascular smooth muscle by opening potassium channels, supressing calcium (Ca^{2+}) entry, and releasing nitric oxide synthase from the coronary artery endothelium.[9] However, epicardial endothelial function can be impaired in patients with myocardial bridging.[10] Angelini *et al.* demonstrated increased spasticity following acetylcholine challenge at the site of myocardial bridging in contrast to vasodilatory response of the normal endothelium.[11] It has been suggested that a similar mechanism is responsible for the spastic response to adenosine due to endothelial dysfunction in the myocardial bridging segment.[12] Increased spastic response was observed in the present case following adenosine throughout the entire cardiac cycle (see Supplementary material online, *Video S2*), supporting the presence of endothelial dysfunction and evidence of underlying ischaemia with positive physiological indices. Thus, full-cycle ratio might be a more useful tool than the other parameters for delineating myocardial bridging-related endothelial dysfunction and ischaemia with concomitant use of adenosine.

Beta-blockers are considered first-line therapy in myocardial bridging, as they reduce the compression of the bridged segment (negative inotropic effect) and increase the diastolic period and diastolic blood flow (negative chronotropic effect).[13] As our patient demonstrated spasm in the presence of adenosine only, we opted to start the patient on a beta-blocker (metoprolol, 25 mg daily). The patient was also on atorvastatin, 20 mg daily. Alternatively, the use of calcium channel blockers targeted at reducing both bridged segment compression and coronary vasospasm can be considered.

Conclusion

Our case highlights the importance of thorough workup of myocardial bridging in symptomatic patients to better understand the underlying physiology and endothelial function after ruling out microvascular disease and consideration of hyperaemic testing if symptoms are suggestive of ischaemia.

Lead author biography

Dr. Sukhdeep Bhogal is an Interventional Cardiology fellow at MedStar Washington Hospital Center. He completed medical school in India and Internal Medicine and Cardiology fellowship at East Tennessee State University. His areas of interest are coronary physiology and imaging and transcatheter aortic valve replacements.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The patient provided written consent to publish the details of the case, in accordance with COPE guidelines.

Conflicts of interest: Sukhdeep Bhogal—None, Hayder Hashim—Consultant: Abbott, Boston Scientific, Philips, CSI; Speakers Bureau: Abbott, Boston Scientific, Philips, CSI, Ron Waksman—Advisory Board: Abbott Vascular, Boston Scientific, Medtronic, Philips IGT, Pi-Cardia Ltd.; Consultant: Abbott Vascular, Biotronik, Boston Scientific, Cordis, Medtronic, Philips IGT, Pi-Cardia Ltd., Swiss Interventional Systems/SIS Medical AG, Transmural Systems Inc., Venous MedTech; Grant Support: AstraZeneca, Biotronik, Boston Scientific, Chiesi, Medtronic, Philips IGT; Speakers Bureau: AstraZeneca; Investor: MedAlliance, Transmural Systems Inc.

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