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A Clinical Approach to Diagnosis and Treatment of Left Anterior Descending Artery Myocardial Bridge

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ABSTRACT

The muscle overlying the intramyocardial segment of an epicardial coronary artery is defined as myocardial bridge (MB). The clinical relevance of MBs is extremely heterogeneous, ranging from incidental finding in asymptomatic patients to different clinical manifestations such as stable or unstable angina, arrhythmias, Takotsubo syndrome or other major cardiovascular events. Moreover, patients can evolve from "asymptomatic carriers" to "symptomatic carriers" over time. In this setting, haemodynamic assessment is challenging and optimal therapy still a matter of debate. This review summarizes epidemiology, pathophysiology, diagnostic work-up (including both morphological and functional assessment) and treatment of patients with MB involving the left anterior descending artery, suggesting a pragmatic clinical approach.

A coronary artery may dip into the myocardium for varying lengths, before reappearing on epicardial surface. The muscle overlying the intramyocardial segment of the coronary artery is termed myocardial bridge (MB), being the artery running within the myocardium referred to as tunneled artery. In 70% to 98% of cases, the MB involves the left anterior descending artery (LAD)[1]. Although MBs are reported to be present in about one-fourth of adults, their true prevalence varies widely according to the diagnostic method used to detect such an anatomic variant. In fact, pathological series reported higher rates of MBs compared to coronary angiography studies, in which MBs were detected as dynamic systolic compression of a coronary segment (milking effect). This mismatch is related to several factors including thickness and length of the MB, reciprocal orientation of coronary artery and myocardial fibers, intrinsic tone of the coronary artery wall, myocardial contractility and heart rate at the time of angiography, and finally observer experience[2-4].

Although the presence of this congenital variant is generally considered a benign condition, patients with MB may present with silent ischemia, stable angina, acute coronary syndromes, Takotsubo cardiomyopathy, and malignant arrhythmias possibly leading to sudden cardiac death[2,5-8]. From a clinical point of view, it is important to understand why some MBs are (or become) symptomatic. In other words, when does a previously asymptomatic patient with a congenital MB become symptomatic? What additional factors unmask or aggravate a MB? Anatomical determinants that need to be taken into account are not only the depth and length of vessel encasement, but also the number of septal branches arising from or near the involved LAD segment. Moreover, pathophysiological factors that may unmask or exacerbate MBs are patient's age, heart rate, left ventricle (LV) hypertrophy, and the presence of coronary

atherosclerosis, since all these may worsen the supply-demand mismatch imposed by the bridge, reducing coronary reserve[9].

The compression of the tunneled segment of the bridged coronary artery may reduce not only the systolic but also the early hyperemic diastolic flow, due to tachycardia, delayed ventricular relaxation and phasic coronary spasm that prolongs also into diastole[10,11]. Moreover, this pathophysiologic phenomenon causes ischemia by "intramural steal" or "branch steal" mechanism, which are linked to decreased perfusion pressure of septal branches and blood suction[12,13]. The disturbed flow pattern observed to the proximal end of the tunneled artery seems to be responsible of the formation and typical distribution of the coronary plaques, which are usually detected 20 to 30 mm proximal to the MB[14,15]. These altered biomechanical forces at the level of the MB could also lead to other potential complications, such as plaque vulnerability/thrombosis, increase in vasospasticity, and intimal injury that may further develop into coronary dissection[16].

Morphological assessment of MBs can be performed with coronary angiography, obtained in different angiographic views to better visualize and characterize the tunneled artery, adjunctive intravascular imaging such as intravascular ultrasound (IVUS), and cardiac computed tomography (CCT). Coronary angiography typically reveals a dynamic systolic milking (≥50% systolic diameter stenosis not present or less evident in diastole) after intracoronary nitrates administration[17,18]. IVUS might improve the detection rate showing the systolic compression with delayed relaxation in diastole of the bridge segment, and the typical "half-moon phenomenon", an echolucent area surrounding the bridge and seen during the whole cardiac cycle. Moreover, IVUS is useful to better characterize the length, thickness, and location of the MB, as well as the presence, severity, and distribution of subangiographic atherosclerosis[19]. Finally, CCT is able to easily detect and characterize MBs, given its 3-dimensional capability and high spatial and contrast resolution. As a matter of fact, CCT can visualize the coronary lumen, the vessel wall, and the myocardial wall, hence allowing accurate definition of the MB's morphological features. The CCT scan protocol is not different from the conventional protocol used to assess coronary artery stenosis and post-processing software is helpful for the precise definition of MB's length and depth[20].

Functional assessment of a bridged coronary artery might be hampered by several factors. Since stenoses in the context of MBs are not fixed and are dependent on the degree of extravascular compression and intramyocardial tension, their invasive assessment should not be limited to resting conditions but should include chronotropic and inotropic stimulation, in order to unmask their ischemic potential. Moreover, differently from fixed stenosis in which the difference between mean and diastolic pressure gradient values across the lesion are not significant, MB may cause significant diastolic pressure gradients but artificially negative systolic pressure gradients secondary to distal pressure overshooting[21]. Granted that, the traditional fractional flow reserve (FFR), a mean of systolic and diastolic pressure gradients, seems largely inadequate for the assessment of the hemodynamic significance of a MB, because systolic pressure overshooting and negative systolic pressure gradients may lead to an underestimation of hemodynamic significance of the bridged segment([21]). To this regard, diastolic FFR was proven to be more sensitive than conventional FFR for the investigation of MBs[22].

Differently from FFR, the instantaneous wave-free ratio (iFR®, Volcano corporation, San Diego, CA, USA) is a lesion-specific, diastolic-only index, which might not be affected by the systolic pressure gradient inversion observed in significant MBs. In addition, the guidewire pull back allows anatomic mapping of the vessel to confirm the step-up at the level of MB[23].

Our group recently analyzed a series of twenty patients with angina and abnormal non-invasive test suggestive of myocardial ischemia, and evidence of MB in the LAD without significant coronary artery disease at coronary angiogram. According to a prespecified protocol, all patients underwent functional evaluation of the MB with FFR and iFR, both at rest and after inotropic stimulus by intravenous dobutamine infusion, to unmask MB ischemic potential[24]. The FFR evaluation was negative at rest in all patients and, after inotropic infusion, when coronary compression was maximal and patients developed symptoms, median FFR did not significantly change compared to baseline[24]. This can be explained by the fact that, in the setting of inotropic stimulation, MBs can cause increase of diastolic but artificially negative systolic pressure gradients secondary to distal pressure overshooting. As previously stated, this phenomenon may produce an artificial elevation in the mean pressure used by traditional FFR (average systole and diastole), resulting in an underestimation of hemodynamic significance of the bridged LAD[21,22]. On the contrary, iFR at rest was abnormal in 65% of our patients with a clear step-up across the MB, as shown by iFR pullback during pressure wire pull back. After inotropic infusion, this index dropped in all cases. Despite the fact that iFR ischemic cut-off values after inotropic infusion are unknown, hemodynamic evaluation of MBs with iFR seems to be more consistent with patients' symptoms and noninvasive test results compared with FFR[24] (figure 1).

Finally, measurement of intracoronary flow velocity and coronary flow reserve by the use of Doppler-tipped guidewires is another useful, but by far less diffused tool to evaluate MB's hemodynamics[25].

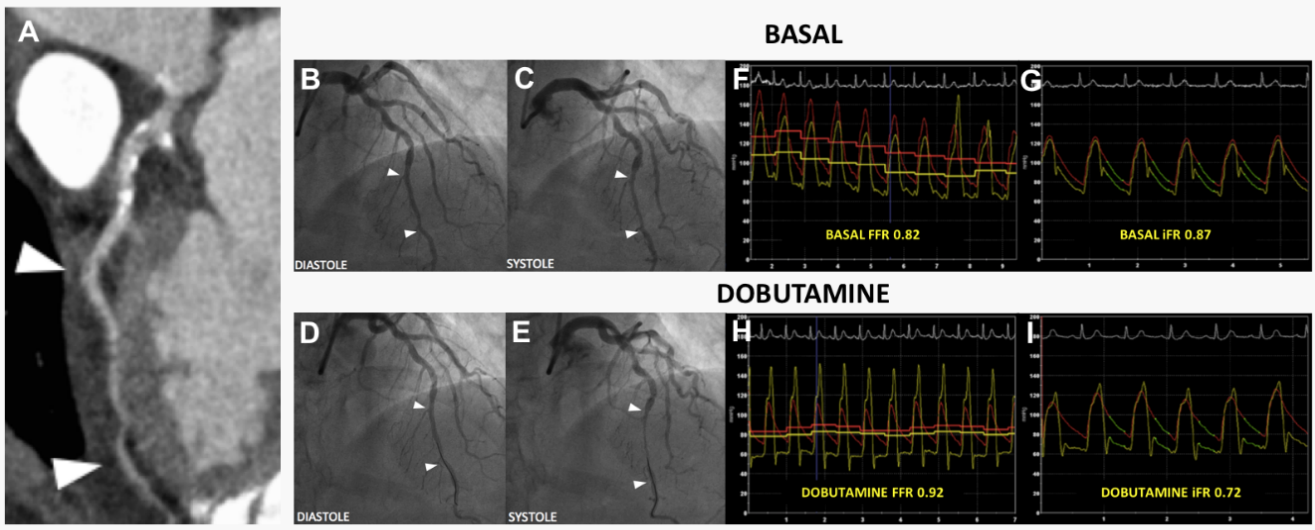

Figure 1: Diagnostic workup of a patient with left anterior descending artery (LAD) myocardial bridge (MB). A: Cardiac computed tomography scan of intramyocardial course of the LAD; note the step-down (top arrow) and step-up (bottom arrow). Angiographic appearance of the LAD MB (arrows), both in systole (B) and diastole, in basal conditions. D, E: Angiographic appearance of the same vessel (arrows), both in systole and diastole, after infusion of dobutamine 20 μ/kg/min. Fractional flow reserve (FFR) measurements are negative (>0.80) before (F) and after (G) dobutamine infusion, whereas diastolic-specific indexes are positive at rest (instantaneous wave-free ratio (iFR))H), and after dobutamine challenge (hyperemic wave-free period pressure ratio) (J).

Among noninvasive imaging tests to evaluate functional ischemic potential of MB are stress echocardiography, stress cardiac magnetic resonance, single-photon emission computed tomography and positron emission tomography[26]. More recently, new post-processing algorithms are available for the derivation of functional information from the anatomic assessment provided by CCT, such as transluminal attenuation gradient and computed tomography (CT)–derived FFR[27,28].

Treatment of patients with a MB should be based on the presence of clinical symptoms and/or objective signs of ischemia. Symptomatic patients seem to respond well to pharmacological therapy, which appears to be the treatment of choice for the vast majority of patients[29,30]. Medical treatment should focus on relieving potential triggers and hemodynamic disturbances that aggravate the MB, such as hypertension/hypertrophy, increased heart rate, reduced diastolic coronary filling period, and inappropriate compression of the coronary artery. Accordingly, b-blockers or calcium-channel antagonists are considered first-line therapy. Ivabradine can be considered in patients with contraindication to beta-blockers or in subjects not at heart rate target (i.e.>70 bpm)[30]. Pure vasodilators, such as nitroglycerin, are not indicated because they can worsen symptoms due to their unfavorable influence on MB hemodynamic[18].

Patients with symptoms refractory to medical therapy can be considered for percutaneous or surgical treatment, which include stent implantation, surgical myotomy and coronary artery bypass grafting (CABG). However, stent implantation in MB is limited due to concerns about higher reported rates of complications, including vessel perforation during stent deployment[31], stent fracture[32], in-stent restenosis[33] and stent thrombosis[34]. Surgical options for MB are more invasive. Potential complications of myotomy include wall perforation, particularly in the case of a deep subendocardial course, ventricular aneurysm formation, and post-operative bleeding[35]. CABG appears to be safe and effective in very selected cases of severely symptomatic patients refractory to other therapies with extensive (>25 mm) or deep (>5 mm) MB[36,37].

Conflict of Interest

Prof Giuseppe Tarantini received lecture fees from St. Jude Medical and Volzano. All other authors have nothing to disclose

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