Evaluation of Coronary Flow Reserve by Myocardial Scintigraphy in Left Ventricular Hypertrophy

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Introduction

The microvascular integrity of the myocardial bed can be assessed by coronary flow reserve (CFR), which is a calculation of the ratio between the absolute coronary blood flow under vasodilator stress and under resting conditions. This measurement is capable of estimating vasomotor dysfunction, and it reflects the hemodynamic effect of focal, diffuse, or small-vessel coronary disease.[1]

Currently, it is possible to measure CFR invasively using the techniques of thermodilution or intracoronary Doppler and through non-invasive methods, such as echocardiography, magnetic resonance imaging, computed tomography, or nuclear medicine.[1]

The gold standard for non-invasive assessment of CFR is positron emission tomography (PET) myocardial perfusion, which has proven to be a valuable diagnostic and prognostic marker in the context of coronary disease and non-obstructive heart diseases.[2] Radiotracers used for PET myocardial perfusion are not usually available in many medical centers worldwide, including Brazil, due to the need for complex and costly logistics of production.

CFR can also be measured by means of conventional myocardial perfusion scintigraphy using special gamma cameras with solid state detectors, known as cadmium-zinc-tellurium (CZT), which are already present in many nuclear medicine services in Brazil. The measurement of CFR using CZT has shown good agreement with PET, and it has a proven impact on prognosis and therapeutic management.[3]

We report a clinical case in which the evaluation of CFR through myocardial scintigraphy using a CZT camera proved to be useful in understanding the pathophysiology of the patient's clinical condition and in stratifying cardiovascular risk.

Keywords:

Myocardial Perfusion Imaging; Hypertrophy, Left Ventricular; Microvascular Angina; Regional Blood Flow.

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Case presentation

We report the case of a 42-year-old, White, male patient with hypertension and overweight, who complained of recurrent atypical chest pain.

He performed an exercise test that presented exclusively electrocardiographic criteria for myocardial ischemia, reaching 95% of the predicted maximum heart rate and 10 metabolic equivalents.

He was referred for myocardial perfusion scintigraphy under physical exertion, which provided evidence of mild myocardial ischemia in the anteroseptal (middle), latero-apical, and inferolateral (middle) segments, with an estimated ischemic burden of less than 5% of the myocardium.

The patient underwent coronary cineangiography, which did not reveal coronary obstructions, but identified an extensive myocardial bridge in the territory of the left anterior descending artery, with a maximum systolic constriction of 70% in the distal third, and signs of left ventricular hypertrophy.

In spite of optimized clinical therapy, the symptoms persisted.

A new myocardial perfusion scintigraphy was performed with assessment of CFR under pharmacological stress with dipyridamole, which provided evidence of pronounced myocardial ischemia of the left ventricle including segments of the apical, lateral, and inferior walls. A relative increase in radiotracer uptake was observed in the apical wall of the left ventricle on the resting images, suggestive of asymmetric ventricular hypertrophy (Figure 1).

CFR assessment (Figure 2) revealed decreased CFR in all vascular territories and reduced total CFR with a value of 0.97, applying values greater than 2.1 as a reference for normality.[4]

A subsequent echocardiographic study confirmed the presence of important mid-apical hypertrophy of the left ventricle, suggestive of Yamaguchi syndrome (Figure 3).

Discussion

More than 20% of patients with angina who undergo invasive assessment of coronary anatomy do not have significant obstructive lesions. However, in the majority of cases, it is possible to identify factors that justify the symptom, such as myocardial bridge or signs of microvascular disease.[5]

Dysfunction of coronary microcirculation has been shown to play a key role in the development and evolution of a series of cardiovascular conditions, whether in obstructive or non-obstructive atherosclerosis, as well as cardiomyopathies of diverse etiologies.[6]

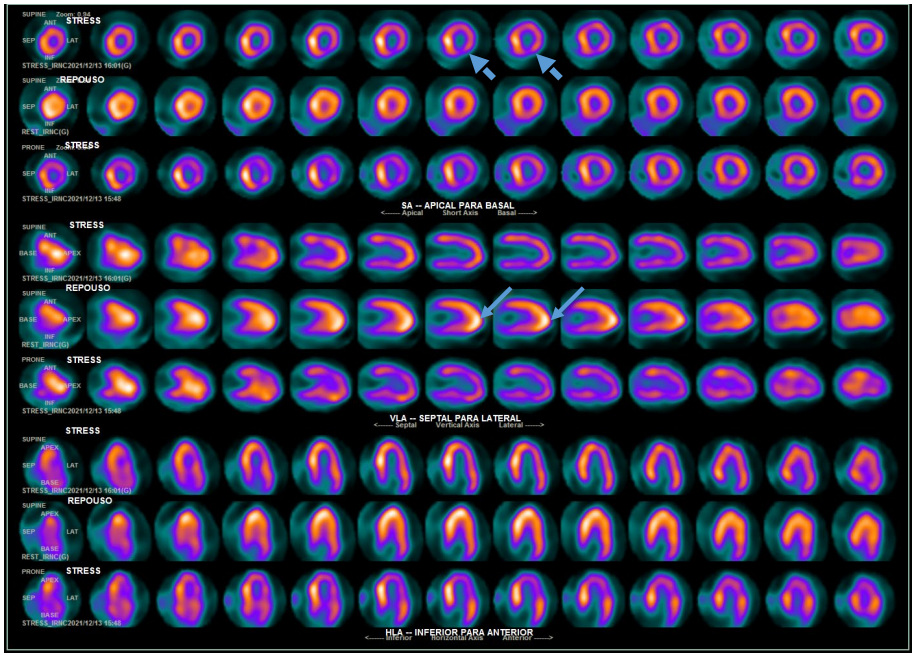

Figure 1 – *Myocardial perfusion scintigraphy. *Images in three axes: short, vertical, and horizontal, respectively. The upper and middle rows show sections in the stress and resting phase with the patient in the supine position, and the bottom row shows sections in the prone position during the stress phase. Short arrows demonstrate areas of perfusion defect in the inferior wall of the left ventricle. The long arrows indicate the relative increase in radiotracer uptake in the apical wall in resting images.*

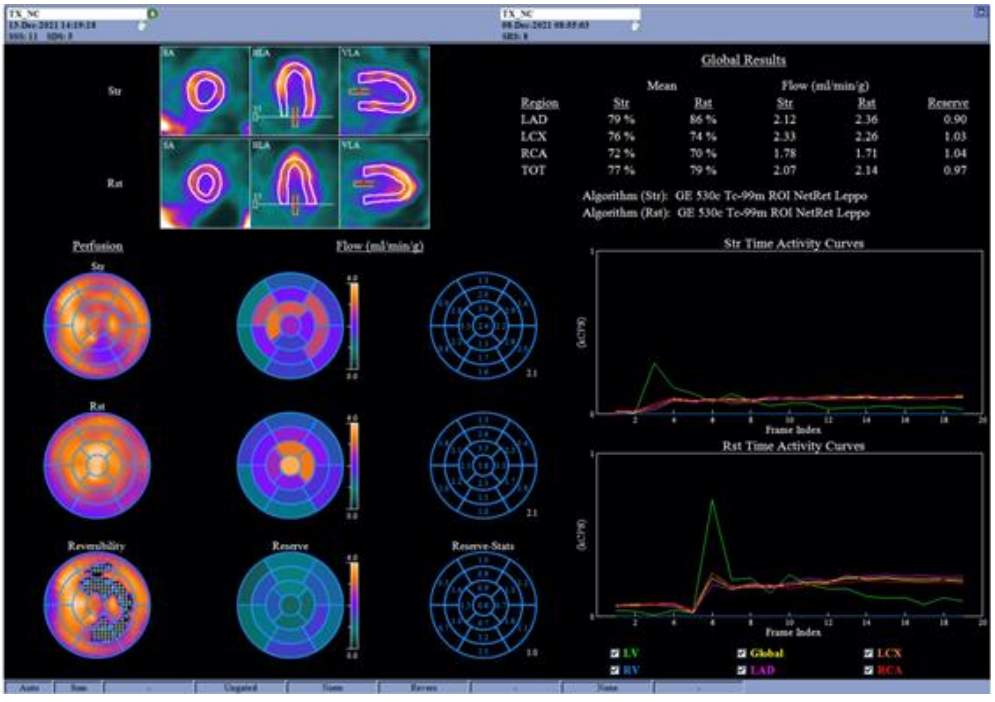

Figure 2 – *CFR assessment. * Upper right: Absolute values of myocardial blood flow under stress and at rest and flow reserve by vascular territory and global reserve. LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; TOT: total values of the left ventricular myocardium. Bottom left: Polar maps condense myocardial perfusion under stress and at rest in the 17 myocardial segments. Reversibility highlights the area of myocardial ischemia. Bottom right: Myocardial radiotracer activity curves over time by vascular territory and globally under stress and at rest.*

Case Report

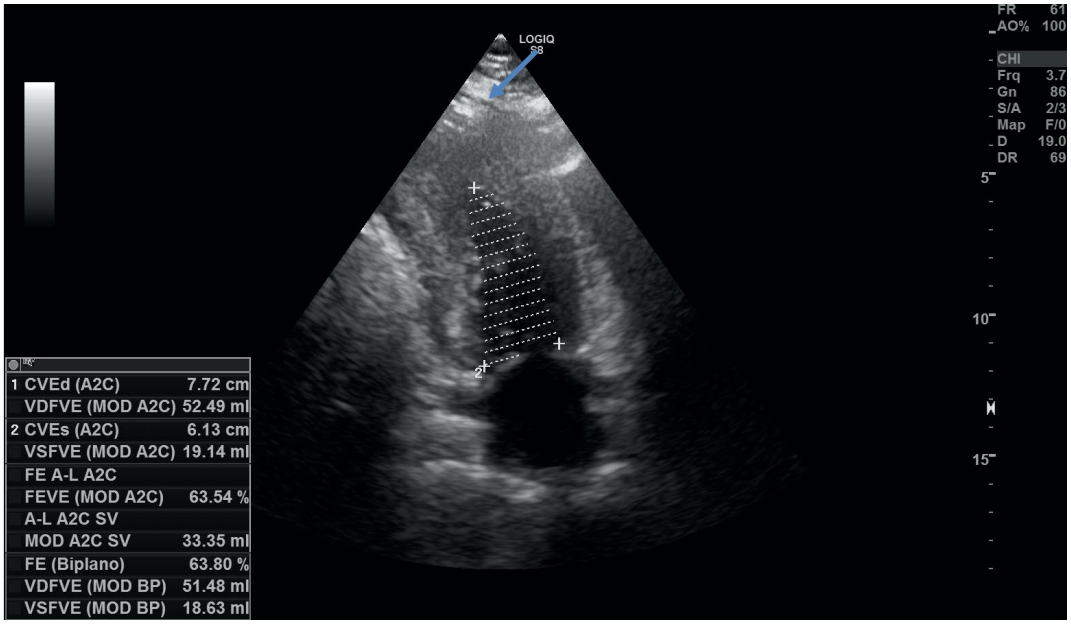

Figure 3 – *Longitudinal two-chamber echocardiogram demonstrating mid-apical left ventricular hypertrophy (arrow).*

Hypertrophic heart disease is a disease of genetic etiology characterized by thickening of the left ventricular wall. It manifests concentrically or asymmetrically, as in apical hypertrophy, also known as Yamaguchi syndrome. Although it is more prevalent among Asian patients, it can be found in up to 10% of cases of left ventricular hypertrophy in patients who are not Asian. Patients with apical hypertrophy may present atrial fibrillation, chest pain, pulmonary hypertension, or ventricular arrhythmias, in addition to an annual mortality rate of up to 4%.[7]

Although magnetic resonance has greater diagnostic sensitivity, echocardiography identifies the disease in the majority of cases, and it can determine prognostic factors, such as the presence of diastolic dysfunction or apical aneurysm.[8]

Myocardial ischemia is a recurrent finding, and it may occur with loss of myocytes and fibrosis. More than the increased demand for oxygen by the hypertrophied myocardium, it is known that structural changes in small vessels are the primary mechanism of perfusion deficit. Thus, damage to the coronary microcirculation is at the core of the ischemic substrate of hypertrophic heart disease.[6]

Studies on the assessment of flow reserve in hypertrophic heart disease have demonstrated the presence of altered CFR, even in areas without hypertrophy, and it plays an important role in prognostic evaluation as a predictor of clinical deterioration, systolic dysfunction, and death, related to the degree of alteration in coronary flow.[9]

In addition to apical ventricular hypertrophy, the patient in this case had a myocardial bridge, a congenital anomaly that determines the intramural course of the coronary epicardial artery. The clinical significance of the myocardial bridge is questionable, considering that it is a systolic compression of the vessel wall, whereas myocardial perfusion is a phenomenon that mainly occurs in diastole. However, the association with ventricular hypertrophy is a determinant additional factor for it reducing myocardial flow reserve and being the cause of angina in these cases.[10]

Evidence has demonstrated that patients with very low global CFR, less than 1.5, without obstructive coronary disease, constitute a high-risk group for cardiovascular events. Unfortunately, the strategies that can alter this clinical outcome are not clear, considering that the pathophysiological mechanisms involved are not completely known.[11]

The assessment of CFR in patients with hypertrophic heart disease, as in the case reported, as well as in other scenarios such as metabolic syndrome, cardio-oncological complications associated with chemotherapy, and heart failure with preserved ejection fraction, identifies the pathophysiological substrate that justifies the patient's clinical condition, stratifies risk, and indicates patients who may benefit from the intensification of the available clinical arsenal with the aim of modifying unfavorable prognosis.[11]

Author Contributions

Conception and design of the research; analysis and interpretation of the data; writing of the manuscript: Félix RCM; acquisition of data: Félix RCM, Pedras FHV, Lima Neto OS, Vitório LM; obtaining financing; critical revision of the manuscript for intellectual content: Pedras FHV.

Potential Conflict of Interest

Renata Christian Martins Félix, Odorico de Souza Lima Neto and Leonardo Medeiros Vitório are collaborators at Clínica Villela Pedras; and Felipe Hermely Villela Pedras is medical director at Clínica Villela Pedras.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Instituto Nacional de Cardiologia under the protocol number 67072022.3.000.5272. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Gould KL. Does Coronary Flow Trump Coronary Anatomy? JACC Cardiovasc Imaging. 2009;2(8):1009-23. doi: 10.1016/j.jcmg.2009.06.004.
2. Gould KL, Johnson NP, Bateman TM, Beanlands RS, Bengel FM, Bober R, et al. Anatomic Versus Physiologic Assessment of Coronary Artery Disease. Role of Coronary Flow Reserve, Fractional Flow Reserve, and Positron Emission Tomography Imaging in Revascularization Decision-Making. J Am Coll Cardiol. 2013;62(18):1639-53. doi: 10.1016/j.jacc.2013.07.076.
3. Petretta M, Storto G, Pellegrino T, Bonaduce D, Cuocolo A. Quantitative Assessment of Myocardial Blood Flow with SPECT. Prog Cardiovasc Dis. 2015;57(6):607-14. doi: 10.1016/j.pcad.2014.12.007.
4. Agostini D, Roule V, Nganoa C, Roth N, Baavour R, Parienti JJ, et al. First Validation of Myocardial Flow Reserve Assessed by Dynamic 99mTc-sestamibi CZT-SPECT Camera: Head to Head Comparison with 15O-Water PET and Fractional Flow Reserve in Patients with Suspected Coronary Artery Disease. The WATERDAY Study. Eur J Nucl Med Mol Imaging. 2018;45(7):1079-90. doi: 10.1007/s00259-018-3958-7.
5. Lee BK, Lim HS, Fearon WF, Yong AS, Yamada R, Tanaka S, et al. Invasive Evaluation of Patients with Angina in the Absence of Obstructive Coronary Artery Disease. Circulation. 2015;131(12):1054-60. doi: 10.1161/CIRCULATIONAHA.114.012636.
6. Del Buono MG, Montone RA, Camilli M, Carbone S, Narula J, Lavie CJ, et al. Coronary Microvascular Dysfunction Across the Spectrum of Cardiovascular Diseases: JACC State-of-the-Art Review. J Am Coll Cardiol. 2021;78(13):1352-1371. doi: 10.1016/j.jacc.2021.07.042.
7. Klarich KW, Jost CHA, Binder J, Connolly HM, Scott CG, Freeman WK, et al. Risk of Death in Long-Term Follow-Up of Patients with Apical Hypertrophic Cardiomyopathy. Am J Cardiol. 2013;111(12):1784-91. doi: 10.1016/j.amjcard.2013.02.040.
8. Hughes RK, Knott KD, Malcolmson J, Augusto JB, Mohiddin SA, Kellman P, et al. Apical Hypertrophic Cardiomyopathy: The Variant Less Known. J Am Heart Assoc. 2020;9(5):e015294. doi: 10.1161/JAHA.119.015294.
9. Cecchi F, Olivotto I, Gistri R, Lorenzoni R, Chiriatti G, Camici PG. Coronary Microvascular Dysfunction and Prognosis in Hypertrophic Cardiomyopathy. N Engl J Med. 2003;349(11):1027-35. doi: 10.1056/NEJMoa025050.
10. Tarantini G, Migliore F, Cademartiri F, Fraccaro C, Iliceto S. Left Anterior Descending Artery Myocardial Bridging: A Clinical Approach. J Am Coll Cardiol. 2016;68(25):2887-99. doi: 10.1016/j.jacc.2016.09.973.
11. Taqueti VR, Di Carli MF. Clinical Significance of Noninvasive Coronary Flow Reserve Assessment in Patients with Ischemic Heart Disease. Curr Opin Cardiol. 2016;31(6):662-9. doi: 10.1097/HCO.0000000000000339.