A novel vessel fraction flow reserve three-dimensional quantitative coronary angiography-based software. First case in Latin America

Novo *software* para reserva de fluxo fracionada tridimensional quantitativa baseado em angiografia coronária. Primeiro caso na América Latina

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ABSTRACT – Fractional flow reserve has become the mainstay of functional hemodynamic assessment and is considered the gold standard to identify ischemic coronary stenoses. However, adopting the method into daily practice has been limited. Indeed, it requires the use of a costly pressure wire and the administration of a hyperemic agent. Vessel fractional flow reserve is a 3D-QCA based fractional flow reserve, using CAAS Workstation (version 8.4; Pie Medical Imaging, Maastricht, the Netherlands). It is a non-invasive method that does not require pressure wire or hyperemic agent; therefore it is time saving and easy to use. This is the first case performed in Brazil and demonstrates the correlation between fractional flow reserve and vessel fractional flow reserve performed in the same lesion, and the feasibility of calculation of vessel fractional flow reserve using 3D QCA-based software. We report the case of a 61-year-old male, who was admitted for typical chest pain. Coronary angiography revealed serial intermediate lesions in the mid- and distal left anterior descending. We evaluated left anterior descending lesions initially by fractional flow reserve then by vessel fractional flow reserve. Fractional flow reserve in distal left anterior descending was 0.65. Then, vessel fractional flow reserve value was calculated at 0.61. In our case, the correlation was adequate and the feasibility with offline calculation was excellent and fast. To the best of our knowledge, this is the first case of vessel fractional flow reserve performed in Latin America. Therefore, we expect vessel fractional flow reserve to be a game changer in management of coronary artery disease patients, particularly those with intermediate lesions.

Keywords: Coronary angiography; Coronary artery disease; Coronary vessels; Fractional flow reserve, myocardial; Blood circulation; Chest pain; Software

RESUMO – A reserva de fluxo fracionada tornou-se o pilar da avaliação funcional hemodinâmica e é considerada o padrão-ouro para identificar estenoses coronárias isquêmicas. No entanto, a adoção do método na prática diária tem sido limitada. Ela requer o uso de um cateter de pressão caro e a administração de agente hiperêmico. *Vessel fractional flow reserve* é uma reserva de fluxo fracionada baseada em 3D-QCA, usando CAAS Workstation (versão 8.4; Pie Medical Imaging, Maastricht, Países Baixos). Trata-se de um método não invasivo, que não requer guia de pressão e nem agente hiperêmico, sendo rápido e fácil de usar. Este é o primeiro caso realizado no Brasil e demonstra a correlação entre reserva de fluxo fracionada e *vessel fractional flow reserve* realizadas na mesma lesão, bem como a viabilidade do cálculo da *vessel fractional flow reserve* por meio do *software* baseado em 3D QCA. Relatamos o caso de um homem de 61 anos, admitido por dor torácica típica. A angiografia coronária revelou lesões intermediárias seriadas nas porções média e distal da artéria descendente anterior. Avaliamos inicialmente as lesões na artéria descendente anterior por reserva de fluxo fracionada e, depois, por *vessel fractional flow reserve*. A reserva de fluxo fracionada na artéria descendente anterior distal foi de 0,65. A seguir, o valor de *vessel fractional flow reserve* foi calculado em 0,61. Em nosso caso, a correlação foi adequada, e a factibilidade com o cálculo *offline*, excelente e rápida. Até onde sabemos, este foi o primeiro caso de *vessel fractional flow reserve* realizado na América Latina. Portanto, esperamos que a *vessel fractional flow reserve* possa ser um marco no tratamento de pacientes coronariopatas, principalmente aqueles com lesões intermediárias.

Descritores: Angiografia coronária; Doença da artéria coronariana; Vasos coronarianos; Reserva fracionada de fluxo miocárdico; Circulação sanguínea; Dor no peito; Software

INTRODUCTION

Invasive coronary angiography has served as the cornerstone for the diagnosis of patients with known or suspected coronary artery disease (CAD). Unfortunately, the technique is limited by inaccuracy of visual estimation to assess the hemodynamic impact of intermediate coronary artery stenosis. This might result in either underestimation or overestimation of CAD severity.¹

Fractional flow reserve (FFR) has emerged as the mainstay of functional hemodynamic assessment of lesions, and is considered the gold standard to identify ischemic coronary stenoses.² Despite indisputable evidence supporting the benefit of FFR to guide clinical decision-making process, its adoption into daily practice has been limited in many countries. Indeed, FFR assessment requires the use of a costly pressure wire or micro-catheter, along with the administration of a hyperemic agent that might cause temporary patient discomfort.³

Although non-hyperemic pressure ratios, such as instantaneous wave-free ratio, resting full-cycle ratio, and diastolic pressure ratio was emerged as adenosine-free faster and easier methods to achieve physiologic assessment, the need for a costly pressure wire remains a fact.^{4,5}

Therefore, a novel non-invasive index using a 3D-QCA based FFR software has emerged. Quantitative flow ratio have been well validated in several studies and it is based on the flow with its limitations.⁶ In the opposite, different 3D-QCA based FFR depending on the pressure are still in investigation.

Vessel fractional flow reserve (vFFR) is a 3D-QCA based FFR, using CAAS Workstation (version 8.4; Pie Medical

Imaging, Maastricht, the Netherlands). This software is based on the pressure drop in a lesion. The advantages of vFFR can be summarized as follows: it is a non-invasive method; it does not requires a pressure wire or a hyperemic agent; and it is time saving and easy to use. Indeed, the software requires only two orthogonal angiograms for the index lesion, and does not depend on X ray. Moreover, vFFR can be applied for several lesions in the same patient, within the same angiogram.⁷

The objective of this study was to present a case in which vFFR was used to evaluate the functional significance of a coronary lesion, comparing it to the gold standard, the FFR. Patient signed an Informed Consent.

CASE REPORT

History

A 61-year-old male with past history of hypertension, dyslipidemia and peripheral artery disease, was admitted for typical exertional chest pain. No abnormality was found on clinical examination. Electrocardiogram and blood tests were normal. Due to the presence of risk factors and the high probability of CAD, coronary angiography was performed.

Diagnosis

Coronary angiography revealed diffuse CAD with serial intermediate lesions (50% to 70%) of mid- and distal left anterior descending (LAD) (Figure 1A). Right coronary artery (RCA) showed severely calcified tandem lesions of the proximal and mid-segments.

vFFR: vessel fractional flow reserve.

Figure 1. (A) Coronary angiogram in right anterior oblique-cran view demonstrated serial left anterior descending intermediate lesions 50% to 70%, mainly in its middle and distal part. (B) Fractional flow reserve (Boston Scientific) value was 0.65 (adenosine intravenous 140mc/kg/minute). (C) Vessel fractional flow reserve calculated at 0.61 with tridimensional modeling of the left anterior descending with the physiology along the artery (Version 8.4, CAAS Workstation Interface, Pie Medical Imaging, Maastricht, the Netherlands).

Procedure

For the revascularization strategy, we decided to evaluate severity of LAD lesions initially by FFR (Boston Scientific, Massachusetts, United States), then by vFFR Software. FFR in distal LAD (post 200mcg intracoronary nitroglycerin and intravenous adenosine 140mc/kg/minute) was 0.65 (Figure 1B), and the pullback showed a diffuse pattern. Next, we calculated vFFR of LAD and compared it with invasive FFR.

We performed two angiograms, avoiding vessel overlapping, with orthogonal angles separated by more than 30°, after intracoronary injection of 200mcg of nitroglycerin. We selected a frame rate of 15 images per seconds. The blood pressure was recorded at this time 140/70mmHg and was inserted in the program, as required. The vFFR value was calculated at 0.61 with a diffuse pattern. In our case, the correlation was adequate and the feasibility with offline calculation was excellent and fast. The patient refused to undergo surgical revascularization. Hence, percutaneous coronary intervention (PCI) for LAD and RCA was scheduled. Rotational atherectomy of RCA was performed with placement of two drug-eluting stents (DES). Thereafter, LAD PCI was completed with one DES implantation. After PCI was completed in LAD, FFR was measured again and was 0.92 – the same value obtained with vFFR post-PCI.

Complete revascularization was achieved with good clinical outcome and symptom relief.

DISCUSSION

As far as we know, this is the first case in Latin America where vFFR was performed, showing a good correlation of the method with invasive FFR. The diagnostic accuracy of vFFR (area under the curve 0.93; 95%CI 0.88-0.97) and the correlation coefficient ($r=0.89$; $p<0.001$) are reassuring and support our findings.

Despite the need of a software license, it is non-invasive index that does not require pressure-wire and adenosine administration, and can be virtually performed in cases of intermediate lesions, by means of payment of a fixed menal fee. Once we perform the angiogram, the software calculates the vFFR automatically, which is also time-saving.

Importantly, the FAST study demonstrated that vFFR determined in a non-invasive fashion, using the novel software, had a high linear correlation with invasively measured FFR; hence, it is a high diagnostic accuracy to detect FFR ≤ 0.80 along with a low inter-observer variability.⁷

The FAST POST study demonstrated that the 3D-QCA derived post PCI vFFR correlates well with invasively measured microcatheter based FFR and has a high diagnostic accuracy to detect FFR <0.90 with low inter-observer variability.⁸

Another study demonstrated in patients with good quality angiographic visualization of left main coronary artery

(LMCA), and available complete LMCA intravascular ultrasound (IVUS) footage, 3D-QCA based vFFR assessment of LMCA disease correlates well to LMCA minimum luminal area as assessed by IVUS.⁹

The multicenter FAST (Fast Assessment of STenosis severity; NCT03791320) study, a prospective observational multicenter study designed to evaluate the diagnostic accuracy of offline 3D-QCA based FFR, using CAAS Workstation (Pie Medical Imaging, Maastricht, the Netherlands) in identifying hemodynamically significant CAD, compared with pressure-wire based FFR (≤ 0.80), is currently ongoing. This multicenter study included only European, American and Asian centers, but not Latin America centers. Moreover, clinical outcome studies should be conducted to analyze the value of vFFR measured by CAAS Workstation, for hemodynamic assessment of lesion severity in daily clinical practice.

Vessel fractional flow reserve is a promising non invasive tool for assessment of intermediate coronary lesions, with good correlation with the gold standard FFR. In Brazil, as well as in other Latin American countries, reimbursement issues for intra-coronary physiology wires have considerably limited their use, despite strong recommendation in the guidelines. Therefore, we expect that vFFR could be a game changer in the management of CAD patients, particularly those with intermediate lesions.

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None.

CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest.

CONTRIBUTION OF AUTHORS

Conception and design of the study: MHR and FR; data collection: MHR, FR and CES; data interpretation: MHR, MB, LAPD, LA, CES and FR; text writing: MHR, MB, LAPD, LA, CES and FR; approval of the final version to be published: MHR, MB, LAPD, LA, CES and FR.

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