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BRIEF COMMUNICATION

Virtual Functional Assessment of Coronary Stenoses Using Intravascular Ultrasound Imaging: A Proof-of-Concept Pilot Study

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Aims We aimed to investigate the performance of virtual functional assessment of coronary stenoses using intravascular ultrasound (IVUS)-based three-dimensional (3D) coronary artery reconstruction against the invasively measured fractional flow reserve (FFR).

Methods and Results Twenty-two (22) patients with either typical symptoms of stable angina or a positive stress test, who underwent IVUS and FFR, were included in this study. Five (5) patients presented FFR values lower than the 0.80 threshold, indicating ischaemia. IVUS-based 3D reconstruction and blood flow simulation were performed and the virtual functional assessment index (vFAI) was calculated. A strong correlation between IVUS-based vFAI and FFR was observed (Spearman correlation coefficient [r_s] = 0.88, $p < 0.0001$). There was a small overestimation of the FFR by the IVUS-based vFAI (mean difference = 0.0196 ± 0.037; $p = 0.023$ for difference from zero). All cases with haemodynamically significant stenoses (FFR ≤ 0.8) were correctly categorised by the IVUS-based vFAI (vFAI ≤ 0.8).

Conclusion The proposed approach allows the complete and comprehensive assessment of coronary stenoses providing anatomic and physiologic information, pre- and post-intervention, using only an IVUS catheter without the use of a pressure wire.

Keywords IVUS • Virtual functional assessment index • FFR

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Introduction

Functional assessment of intermediate-grade coronary stenoses using fractional flow reserve (FFR) is valuable for the management of stable coronary artery disease [1]. Intravascular ultrasound (IVUS) imaging provides significant anatomic information for the guidance of percutaneous coronary intervention but the IVUS-based anatomic measures of lesion severity do not correlate well with FFR [2]. The high cost, additional procedure time and the incremental risk during the intervention are among the main factors which preclude the regular use of both FFR and IVUS in the same patient in the catheterisation laboratory. Recently, the use of 3D quantitative coronary angiography (3D-QCA) coupled with computational fluid dynamics (CFD) has been proposed for virtual functional assessment of stenoses [3,4], but a similar approach using IVUS images has not been previously studied.

In the current work, we aimed to investigate the performance of virtual functional assessment of coronary stenoses using IVUS-based 3D coronary artery reconstruction and computational fluid dynamics against FFR measured using the pressure wire.

Methods

Twenty-two (22) patients (15 left anterior descending arteries, 5 right coronary arteries and 2 left circumflex arteries) who presented with either typical symptoms of stable angina or a positive stress test, had preserved ejection fraction, and underwent both IVUS imaging and FFR measurement of the same artery were included in the current study. Intravascular ultrasound imaging was performed by using a motorised pullback device (constant speed of 0.5 mm/sec) with either a phase-array 20 MHz transducer (16 arteries; Volcano Corporation, Rancho Cordova, CA-16 arteries) or a mechanical 40 MHz transducer (6 arteries; OptiCross, Boston Scientific Corporation, MA, USA). Fractional flow reserve was measured using a pressure wire (ComboWire XT, Volcano Corporation, CA, USA or PressureWire Aeris, St Jude Medical, MN, USA) according to standard clinical practice. The lumen borders derived from end-diastolic IVUS images were stacked linearly in order to rebuild the lumen geometry in 3D space (Figure 1C).

To obtain a virtual estimate of FFR using our IVUS-based 3D models, we computed the virtual functional assessment index (vFAI), which has been previously shown to be accurate against FFR in angiography-based (3D-QCA) coronary models [3]. Briefly, the obtained IVUS-based geometries were processed with CFD techniques involving the generation of a finite volume mesh, which enables the solution of the 3D transport equations governing the conservation of mass and momentum (ANSYS, PA, USA). Then, vFAI was computed on the basis of the artery-specific pressure gradient–flow relationship as previously described [3]. Figure 1A-D demonstrates a representative case with an ischaemia-producing lesion and the corresponding vFAI. Twenty (20) minutes per vessel was the average time required for our IVUS-based vFAI approach.

Results

In the 22 cases studied, the mean FFR was 0.87 ± 0.09, and five cases had FFR ≤ 0.8 indicating functionally significant stenoses. There was a close correlation between IVUS-based vFAI and FFR (Spearman correlation coefficient $[r_s] = 0.88$, $p < 0.0001$; Figure 1E). The Bland-Altman plot showed a mean difference of 0.0196 ± 0.037 ($p = 0.023$ for difference from zero; Figure 1F) indicating that vFAI slightly overestimates on average the FFR (3). All five cases with functionally significant stenoses (FFR ≤ 0.8) were correctly categorised by the IVUS-based vFAI (vFAI ≤ 0.8). In our very small sample size, the diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of the IVUS-based vFAI ($\leq$0.80) against FFR ($\leq$0.80) were 95.5, 100, 94.1, 83.3 and 100%, respectively.

Discussion

Our results demonstrate for the first time the feasibility of using routine intravascular imaging for virtual functional assessment of coronary stenoses. Previous studies have shown that anatomic indices (e.g. minimum lumen area) derived from IVUS or optical coherence tomography have a mediocre correlation with FFR and cannot be used in routine practice for identifying functionally significant stenoses with a high diagnostic accuracy [2,5]. Our approach differs from previous studies, making use of the cross-sectional intravascular images for performing blood flow simulation, thereby providing the pressure distribution across a lesion. Although our method neglects the curved geometry of the coronary arteries on the epicardial surface, our results suggest that the 3D curvature does not have a major impact on the pressure distribution, and thus, this limitation may not be critical for accurate virtual functional assessment of coronary stenoses.

Conclusions

The proposed approach provides both anatomic and physiologic information, thereby enabling complete and comprehensive assessment of coronary lesions pre- and post-intervention using one intravascular imaging catheter without requiring the pressure wire. These observations may have important clinical implications in routine practice, and warrant further investigation in a larger clinical setting in order to appropriately assess the diagnostic performance of the proposed approach.

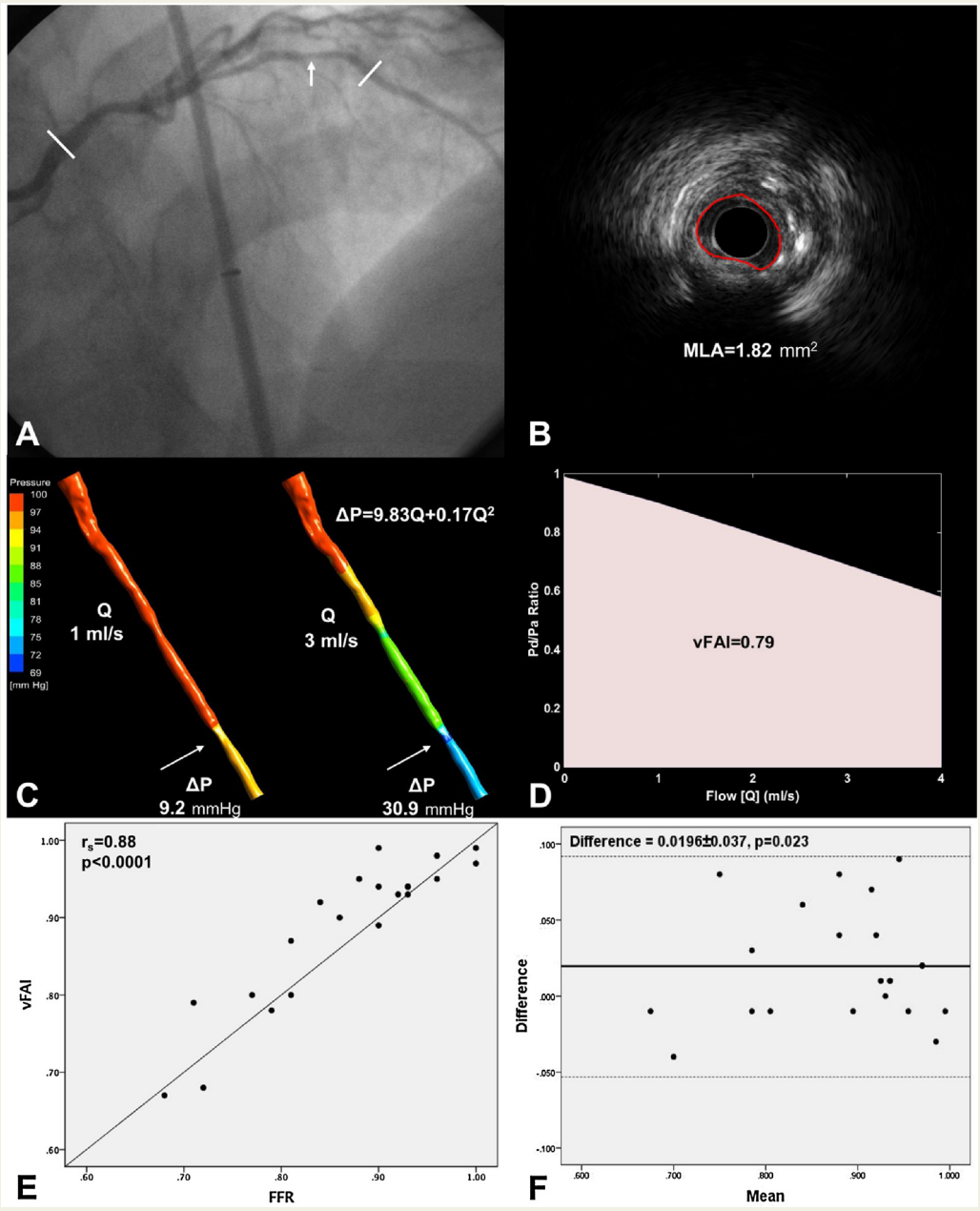

Figure 1 **A.** Angiographic image of a left anterior descending artery with a functionally significant lesion assessed by fractional flow reserve (0.71). The two straight lines indicate the proximal and distal ends of the segment interrogated by intravascular ultrasound (IVUS). The arrow indicates the location of the minimum lumen area. **B.** IVUS image corresponding to the minimum lumen area (1.82 mm^2) of the lesion. **C.** Three-dimensional coronary lumen reconstruction after linearly stacking the lumen borders of the IVUS images. A colour map denotes the pressure distribution for the simulated rest and hyperaemic flow rates which are used for the computation of the virtual functional assessment index (vFAI). The arrow denotes the location of the minimum lumen area shown in the IVUS image. **D.** Relationship between the ratio of distal to aortic pressure (P_d/P_a) and flow for the studied artery, and calculation of the virtual functional assessment index as the ratio of the area under the curve to the total area. **E.** There was a close correlation between the IVUS-based vFAI and fractional flow reserve (FFR; r_s = 0.88). **F.** The Bland-Altman plot showed a mean difference of 0.020 (solid line) between vFAI and FFR; the dashed lines represent the values at mean ± 1.96SD. Of note, 20 plotted values are shown in graphs E and F due to overlapping of cases with identical FFR and vFAI values (i.e. there were two cases with FFR = 0.96 and vFAI = 0.98, and another two cases with FFR = 0.93 and vFAI = 0.94).

Conflict of Interest Statement

None of the authors declares any conflict of interest.

References

[1] De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PAL, Piroth Z, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. N Engl J Med 2012;367:991–1001.

[2] Waksman R, Legutko J, Singh J, Orlando Q, Marso S, Schloss T, et al. FIRST: fractional flow reserve and intravascular ultrasound relationship study. J Am Coll Cardiol 2013;61:917–23.

[3] Papafaklis MI, Muramatsu T, Ishibashi Y, Lakkas LS, Nakatani S, Bourantas CV, et al. Fast virtual functional assessment of intermediate coronary lesions using routine angiographic data and blood flow simulation in humans: comparison with pressure wire — fractional flow reserve. EuroIntervention 2014;10:574–83.

[4] Tu S, Barbato E, Koszegi Z, Yang J, Sun Z, Holm NR, et al. Fractional flow reserve calculation from 3-dimensional quantitative coronary angiography and TIMI frame count: a fast computer model to quantify the functional significance of moderately obstructed coronary arteries. JACC Cardiovasc Interv 2014;7:768–77.

[5] Gonzalo N, Escaned J, Alfonso F, Nolte C, Rodriguez V, Jimenez-Quevedo P, et al. Morphometric assessment of coronary stenosis relevance with optical coherence tomography: a comparison with fractional flow reserve and intravascular ultrasound. J Am Coll Cardiol 2012;59:1080–9.