

Noninvasive CT-based hemodynamic assessment of coronary lesions derived from fast computational analysis: a comparison against fractional flow reserve

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Abstract

Objectives

Application of computational fluid dynamics (CFD) to three-dimensional CTCA datasets has been shown to provide accurate assessment of the hemodynamic significance of a coronary lesion. We aim to test the feasibility of calculating a novel CTCA-based virtual functional assessment index (vFAI) of coronary stenoses $>30\%$ and $\leq 90\%$ by using an automated in-house developed software and to evaluate its efficacy as compared to the invasively measured fractional flow reserve (FFR).

Methods and results

In 63 patients with chest pain symptoms and intermediate (20-90%) pre-test likelihood of coronary artery disease undergoing CTCA and invasive coronary angiography with FFR measurement, vFAI calculations were performed after 3D reconstruction of the coronary vessels and flow simulations using the Finite Element Method. A total of 74 vessels were analysed. Mean CTCA processing time was $25(\pm 10)$ minutes. There was a strong correlation between vFAI and FFR, ($R=0.93$, $p<0.001$) and a very good agreement between the two parameters by the Bland-Altman method of analysis. The mean difference of measurements from the two methods was 0.03 (SD=0.033), indicating a small systematic overestimation of the FFR by vFAI. Using a receiver-operating characteristic curve analysis, the optimal vFAI cut-off value for identifying an FFR threshold of ≤ 0.8 was ≤ 0.82 (95% CI: 0.81 to 0.88).

Conclusions

vFAI can be effectively derived from the application of Computational Fluid Dynamics to three-dimensional CTCA datasets. In patients with coronary stenoses severity $>30\%$ and $\leq 90\%$, vFAI performs well against FFR and may efficiently distinguish between hemodynamically significant from non significant lesions.

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Keywords: coronary artery disease, fractional flow reserve, computed tomography coronary angiography

Key Points:

- Virtual functional assessment index (vFAI) can be effectively derived from 3-D CTCA datasets.
- In patients with coronary stenoses severity $>30\%$ and $\leq 90\%$, vFAI performs well against FFR.
- vFAI may efficiently distinguish between functionally significant from non-significant lesions.

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6 **INTRODUCTION**
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8 Fractional flow reserve (FFR) has evolved as the invasive reference standard for functional
9 assessment of coronary stenoses and guidelines recommend its routine application in patients
10 undergoing ICA in the absence of previously non-invasively documented significant inducible
11 ischemia [1]. In patients with stable CAD, FFR does not substitute the assessment of inducible
12 myocardial ischemia, but it has proven to be superior to classical coronary anatomic parameters
13 (i.e. stenosis severity) in guiding patients' management, reliably discriminating the coronary
14 lesions which have hemodynamic significance and could be revascularized from those that can be
15 safely managed conservatively, with improved patients' clinical outcome and overall resource
16 utilization [1-3]. Nevertheless, FFR is not routinely performed in daily clinical practice, being used
17 in less than 10% of the coronary diagnostic or interventional procedures [4], possibly due to added
18 technical needs (i.e. need for a dedicated wire and administration of a coronary vasodilator) and
19 higher cost (8).
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21 In the last decade, computed tomography coronary angiography (CTCA) has become a valid
22 diagnostic tool in different patient groups, allowing accurate non-invasive evaluation of CAD
23 extent and severity [5, 6]. Moreover, by application of computational fluid dynamics (CFD) to
24 coronary three-dimensional anatomical models, it has been demonstrated that CTCA allows also
25 non-invasive assessment of the hemodynamic relevance of a coronary lesion with good diagnostic
26 accuracy compared to invasive FFR [7-13]. A number of recent studies have suggested that
27 quantitation of CTCA-based FFR (FFR_{CT} - HeartFlow, Inc., Redwood City, CA) might
28 significantly increase the diagnostic accuracy of CTCA [14-21]. However, the current version of
29 this technique requires a remote and lengthy core-laboratory analysis which could limit its wider
30 clinical application. Kruk *et al.*, proposed an alternative method using a software research
31 prototype (cFFR version 1.4, Siemens AG Healthcare, Forchheim, Germany), which does not
32 require a remote core-laboratory analysis [9, 22, 23], while Ko *et al* developed a method which
33 still requires a core-laboratory analysis (~~Canon Toshiba~~-Medical Systems Corp.), but is fast with a
34 computational time around 30 minutes [13].
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6 The evaluation of virtual functional assessment index (vFAI) measured from invasive angiographic
7 data [24] has been recently suggested as a valid alternative to FFR measurements in patients
8 submitted to ICA, allowing to determine the hemodynamic relevance of a given coronary lesion
9 with a few minutes long computation time. The algorithm uses three-dimensional (3D) coronary
10 anatomical data and steady-flow CFD analysis to compute the ratio of distal to proximal pressure
11 over the lesion for flows in the range of 0 to 4 ml/s, normalized by the ratio over this range for a
12 normal artery, offering a measure of CAD hemodynamic significance that is numerically equal to
13 the invasively measured FFR.
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18 However, while vFAI measures have been successfully derived from 3D-ICA datasets, positively
19 mimicking invasive FFR results, the possibility to compute this coronary functional parameter from
20 CTCA-based coronary anatomical models has not yet been investigated. The first aim of the current
21 study is to test the feasibility of assessing vFAI by using our automated in-house developed CTCA
22 3D reconstruction software for generating 3D arterial models, and performing the required blood
23 flow simulations on the aforementioned models [25]. The second aim is to evaluate the efficacy of
24 our method by comparing the derived vFAI values to the invasively measured FFR in coronary
25 stenoses ranging between 30%-90%.
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33 34 35 **MATERIALS AND METHODS**

36 *Study population*

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39 This is a retrospective analysis based on the FP7 multicentre EVINCI (EValuation of INtegrated
40 Cardiac Imaging for the Detection and Characterization of Ischaemic Heart Disease) project and
41 part of the on-going Horizon-2020 SMARTool (Simulation Modeling of coronary ARtery disease:
42 a tool for clinical decision support) project. The complete EVINCI protocol is available at
43 <http://www.clinicaltrials.gov> (NCT00979199). Dedicated core-labs were responsible for
44 harmonization of imaging protocols, quality assessment of imaging tests and independent imaging
45 analysis. From the whole EVINCI population we identified 69 patients with intermediate
46 probability (20-90%) of CAD, who underwent both CCTA and ICA demonstrating coronary
47 stenoses with 30-90% luminal reduction of a major vessel and in whom invasive FFR was assessed.
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6 Patients with previous acute coronary syndrome, known CAD, left ventricular ejection fraction
7 <35%, more than moderate valve disease, and cardiomyopathy were excluded. From the enrolled
8 patients, those with ~~From this group, patients with~~ satisfactory-to-excellent image quality of CTCA
9 acquisition as defined by the EVINCI CTCA core-lab, based on absence of motion artifact, image
10 noise or extensive coronary calcifications, were selected for evaluating the accuracy of vFAI
11 compared to invasive FFR to predict the presence of hemodynamically significant CAD.
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13 Accordingly, from the 69 patients, 6 (8.7%) were excluded from the study due to poor image
14 quality.

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Invasive coronary angiography and FFR measurements

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23 ICA was performed using standard techniques and multiple projections. Quantitative analysis by
24 ICA core-lab was available in all the selected patients. The FFR was invasively measured using a
25 Combo-Wire (Volcano Therapeutics, Rancho Cordova, California), under the administration of
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27 140 µg/kg/min of intravenous adenosine. Segments with FFR values ≤0.8 were considered to
28 indicate significant stenoses.
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CTCA acquisition protocol

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37 ~~Coronary CTCA was performed using ≥64-slice CT scanners.~~ Coronary CT angiography was
38 performed in all of the enrolled patients, as mandated by the original protocol of the EVINCI study
39 [26], using ≥64-slice CT scanners. The arterial segments of interest were reconstructed in mid to
40 end diastole (70%–80% of the R-R interval) with an average slice thickness of 0.6 mm and an
41 increment of 0.6 mm. To optimize image acquisition and final CTCA quality, beta-blockers and
42 sub-lingual nitrates were used as per study protocol. In order to improve the interpretability of CT
43 images and maximize the use of dose-sparing prospective ECG-gating, a regular heart rate of <65
44 bpm was adopted by the study protocol. Accordingly, the use of beta-blockers was encouraged in
45 case of higher heart rates, by means of up to 25 mg of intravenous metoprolol.

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6 The presence of coronary calcifications was evaluated in each patient by computation of calcium
7 score (CACS), which was considered extensive if it was higher than 400 [26]. Scan quality of the
8 CTCA was categorized by the independent EVINCI Core-Lab into 4 categories (i.e. excellent,
9 good, satisfactory and poor). Scans of poor quality were excluded from the present analysis.
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12 13 **CTCA 3D Reconstruction**

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15 The 3D reconstruction was performed using our in-house developed software and the
16 reconstruction process is carried out in 7 steps, as it is described elsewhere [25].
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19 Coronary arteries were reconstructed using the same landmarks for each patient based on the
20 SYNTAX SCORE chart. Specifically, for RCA, the reconstructed models included segments 1–3,
21 for the LAD artery, segments 6–8, whereas for the LCx artery, segments 11–13. The reconstruction
22 and the vFAI calculation process are depicted in Fig. 1 (A-E).
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26 27 **Virtual Functional Assessment Index (vFAI) calculation**

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29 Blood flow simulations were performed on the 3D models of the arteries by generating a mesh of
30 tetrahedral finite elements which then allows the solution of the appropriate Navier-Stokes and
31 continuity equations using ANSYS® CFX 15 (Canonsburg, USA).
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35 For the vFAI calculation, following the method of Papafaklis *et al.* [24], we performed two separate
36 simulations for each case, applying flow rates of 1 and 3 ml/s, in order to create the case-specific
37 pressure gradient (ΔP)-flow relationship [27] for each case (Eq. 1):
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$$41 \quad \Delta P = 0 + f_v Q + f_s Q^2 \quad (1)$$

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43 where ΔP is the pressure gradient, Q is the flow rate, f_v is the coefficient of pressure loss due to
44 viscous friction and f_s is the coefficient of pressure loss due to flow separation [28-30]. By solving
45 the fully determined system of the aforementioned equation, we calculated P_d/P_a from (Eq. 2):
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$$49 \quad \frac{P_d}{P_a} = 1 - f_v \frac{Q}{P_a} - f_s \frac{Q^2}{P_a} \quad (2)$$

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51 P_a was set at 100 mmHg (mean aortic pressure), hence the area under the P_d/P_a vs. flow curve is
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6 then calculated for a flow range between 0 and 4 ml/s, which corresponds to the mean+2SD
7 increase of the hyperaemic flow rate in a normal human coronary artery, initiating from an average
8 flow rate value of 1 ml/s during rest [31]. Finally, we calculated the vFAI for each case as the ratio
9 of the area under the artery-specific P_d/P_a vs. flow curve to the reference area, a value that has been
10 shown to correlate well to the invasively measured FFR value [24]. Although vFAI was tested and
11 validated on ICA derived 3D arterial models, the fluid dynamics background of the aforementioned
12 method may also be applicable to CTCA derived models, since it takes into account only the
13 geometry itself of the model of interest and not other hemodynamic or biological factors.
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20 Image analysis was performed without prior knowledge of the FFR or ICA values by an
21 independent reader (PS) with experience in analysing CTCA images and using the 3D
22 reconstruction module optimally. In vessels with multiple lesions, the precise segment of vFAI
23 measurement was selected by an independent reader (MIP) not involved in the vFAI analysis to
24 match carefully the respective ICA segment on which invasive FFR was measured. To test
25 interobserver agreement, the same analysis was performed in a randomly selected subset of studies
26 by a second reader (DL) following appropriate training. The average analysis time required for
27 each of the assessed arteries was 25 minutes (\pm 10 minutes). The required average 3D
28 reconstruction time was around 3 minutes and the remaining was needed for the necessary blood
29 flow simulations. Two examples, one of a rather borderline case and one severely ischemic are
30 depicted in Fig. 2.
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40 *Statistical analysis*

41 The relationship between FFR and vFAI was quantified by calculating the Pearson's correlation
42 coefficient. Bland-Altman plots and the corresponding 95% limits of agreement were used to assess
43 the agreement between the two methods. ROC analysis was performed for identifying the cut-off
44 values of the examined variables. Categorization of FFR and vFAI values was made using the cut-
45 off of 0.8 and the calculated cut-off from ROC curve for the FFR and vFAI, respectively. ANOVA
46 was used for multiple group comparisons followed by Bonferroni correction where applicable.
47 Sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV),
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6 and diagnostic accuracy (the percentage of patients correctly diagnosed by vFAI) were used to
7 assess the performance of vFAI. P values <0.05 were considered statistically significant.
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9 Comparison ROC curves was based on the DeLong method (MedCalc software). The McNemar
10 test was used to compare the accuracy of vFAI and CCTA to predict ischemia causing stenosis. P
11 values <0.05 were considered statistically significant.

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17 RESULTS

19 *Baseline characteristics of the study population*

21 The population of the present study included 63 patients (mean age 62.9 ± 7 years, 61 % males)
22 with stable symptoms. Hypercholesterolemia, hypertension and CAC score > 100 were present in
23 more than 60% of patients. The mean heart rate during the CTCA scans was 60 ± 7 beats/min.
24 Patients' characteristics are summarized in Table 1. A total of 74 coronary arteries with coronary
25 stenoses ranging from 30–90% at quantitative ICA were interrogated by invasive FFR. The RCA
26 was involved in 17 (25.5%), whilst the LAD and LCx in 42 (52.9%) and 15 (21.6%) of cases
27 respectively. Thirty-five (47.3%), 31 (41.9%), and 8 (10.8%) coronary arteries had a 30-49%, 50–
28 70%, and 70-90% stenosis, respectively. FFR >0.8 was recorded in 50 vessels (67.5%), 0.75-0.80
29 in 9 (12.2%) and ≤ 0.75 in 15 (20.3 %) vessels respectively.

39 **CTCA derived vFAI measurements and FFR**

41 CTCA scan quality was defined as good–excellent for 65 (87.8%) coronary arteries and satisfactory
42 for 9 (12.2%) vessels. The interobserver agreement for vFAI measurements was tested in 11
43 randomly selected coronary vessels (4 RCA, 7 LAD) (8 of good–excellent and 3 of satisfactory
44 quality). There was a strong agreement between the two observers with no significant difference
45 in vFAI values (mean difference=0.0046, SD=0.028, p=0.29). The intraobserver agreement for
46 vFAI measurements was tested in 37 randomly selected coronary vessels (8 RCA, 21 LAD, 8 LCx)
47 (31 of good–excellent and 6 of satisfactory quality). There was a strong agreement between the
48 two measurements with insignificant difference in vFAI values (mean difference= 0.0008,
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6 SD=0.006, p=0.41). FFR declined as stenosis severity increased (ANOVA p=0.003). Specifically,
7 FFR was lower (0.74±0.1) in vessels with stenoses 70–90% compared to those with stenosis
8 severity 50–69% (0.83±0.08, p=0.033) and 30–49% (0.86±0.08, p=0.02). No statistically
9 significant difference was observed in FFR values derived from vessels with stenosis severity 30-
10 49% compared to those with 50-69% diameter stenosis (p=0.55). vFAI similarly declined as
11 stenosis severity increased (ANOVA p=0.015). vFAI was lower (0.79±0.1) in vessels with stenoses
12 70-90% compared to those with stenosis severity 50-69% (0.87±0.09, p=0.048) and 30-49%
13 (0.88±0.07, p=0.012). No statistically significant difference was observed in vFAI values derived
14 from vessels with stenosis severity 30-49% compared to those with 50-69% diameter stenosis
15 (p=1.0).

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18 There was a strong correlation between vFAI and FFR (R=0.93, p<0.001) and a very good
19 agreement between the two parameters by the Bland-Altman method of analysis (Fig. 2). The mean
20 difference of measurements was 0.03 (SD=0.033, p<0.0001), indicating a small systematic
21 overestimation of the FFR by vFAI. The corresponding limits of agreement were from -0.03626 to
22 0.09599, with 95% confidence intervals of -0.04968 to -0.02284 for the lower limit and 0.08257 to
23 0.1094 for the upper limit. Agreement was unaffected by calcification level. For calcified vessels
24 with Agatston Score>400, (n=23) the mean difference was 0.036±0.065, whereas for milder
25 calcifications (Agatston Score<400, n=51), the mean difference was 0.036±0.047.

26 ***Diagnostic accuracy of vFAI***

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28 Using a receiver-operating characteristic curve (ROC) analysis, the optimal vFAI cut-off value for
29 identifying an FFR threshold of ≤0.8 was ≤0.82 (95% CI: 0.81 to 0.88). Fig. 3 shows the ROC
30 curves comparing the diagnostic accuracy of vFAI and traditional CTCA analysis (stenosis ≥ 50%)
31 to identify a coronary lesion with FFR ≤ 0.8. Using a threshold of <0.80 as the FFR cut-off value
32 for hemodynamically significant lesions, the overall diagnostic performance of vFAI further
33 increases, while that of CTCA decreases. The overall diagnostic performance of vFAI and CTCA
34 for both FFR thresholds (i.e. ≤0.80 and <0.80) is presented in Table 2. The diagnostic accuracy of
35 vFAI was significantly higher than CCTA (93.2% vs. 52.7%, p=0.0027).

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8 **DISCUSSION**
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10 We have demonstrated the feasibility of deriving an accurate index of hemodynamically significant
11 coronary lesions through non-invasive quantitation of CTCA-based vFAI. Specifically, in a
12 population of patients with intermediate probability of CAD and stenosis severity ranging from
13 30% to 90%, vFAI could be readily obtained within a short computation time, well matching the
14 results of the accepted gold-standard represented by invasive FFR. A cut off vFAI value of ≤ 0.82
15 was associated with high sensitivity, specificity and NPV (87.5%, 96% and 94.1%, respectively)
16 for identifying lesions with $FFR \leq 0.8$. An FFR cut-off value < 0.80 resulted in even higher
17 sensitivity and NPV [32].

18 A number of studies have already reported the ability of CTCA derived functional indexes to
19 mimic invasive FFR measurements for the detection of hemodynamically significant CAD [7, 17,
20 33]. In particular, while initial reports had suggested the existence of only a moderate agreement
21 between FFR_{CT} and invasive FFR [12], recent refinements of computational techniques and CFD
22 modelization have improved the accuracy of FFR_{CT} in unmasking the presence of
23 hemodynamically significant coronary lesions and quantifying their severity [33]. Our results
24 show that vFAI slightly overestimates FFR but can distinguish functionally significant from non-
25 significant lesions with high specificity and NPV. In our study population, the cut off vFAI value
26 of 0.8, which has been used in prior studies, would have resulted in a low sensitivity (66.7 %). Due
27 to the slight overestimation of FFR by vFAI demonstrated in the present study, the best cut off
28 value for vFAI was ≤ 0.82 , which increased sensitivity to levels comparable to those of similar
29 studies without affecting significantly the specificity. Our results also demonstrate that for studies
30 of adequate quality, coronary calcification did not affect significantly the agreement between vFAI
31 and FFR. Intense calcification affects image quality by creating the so-called “blooming effect”
32 leading to an overestimation of the arterial lumen and thus restricting data analysis only to studies
33 without obvious artefactual effects. We are currently working to resolve these issues by developing
34 a dedicated “blooming removal” algorithm and further denoising filters.
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6 Today's advanced computational methods are based on modeling of the physiological parameters
7 of coronary microcirculation and vascular resistance and their influence in coronary flow during
8 hyperemia. Considering that virtual functional assessment reflects only vessel geometry-related
9 changes without taking into account alterations at the microcirculation level, slight disagreement
10 between ours and other FFR_{CT} techniques regarding the optimal threshold for disease detection
11 should be expected. The same holds true for comparisons between vFAI and ICA-FFR.
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16 Previous studies found that FFR_{CT} slightly underestimates the actual FFR values (mean difference
17 between FFR-FFR_{CT}: Kruk *et al.*: +0.01, Koo *et al.*: +0.022, Min *et al.*: +0.058 and Norgaard *et al.*:
18 +0.03) [7, 9, 17, 33]. These studies use a different approach regarding the calculation of FFR_{CT},
19 where the entire coronary vasculature is reconstructed in 3D and the lumped parameter models of
20 the microcirculation to the outflow boundaries are coupled but at the expense of increased
21 computational time and need of strong computational power. Using another approach, Taylor *et*
22 *al.* [34], computed the vascular resistance and calculated the LV mass for estimating FFR. Despite
23 the small overestimation of FFR compared to the aforementioned studies, our diagnostic accuracy
24 is not inferior to them. In particular, diagnostic accuracy, sensitivity, specificity, PPV, and NPV
25 for a per-vessel analysis for vFAI were 93.2%, 87.5%, 96%, 91.3% and 94.1% whereas for FFR_{CT}
26 77.1%, 56.1%, 92.7%, 85.2% and 73.9% for the study by Kruk *et al.* [9] (for a stenosis range of
27 50%-90%).
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36 ***Clinical implications***

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39 A preemptive non-invasive evaluation of the presence of hemodynamically significant CAD is
40 favored by current clinical guidelines for avoiding unnecessary coronary interventions [35]. Whilst
41 different cardiac imaging tests can be used to rule out the presence of functionally significant
42 CAD, a significant proportion of patients currently submitted to ICA still show no
43 hemodynamically significant coronary lesions [36]. Many of these patients have coronary
44 atherosclerosis that can be depicted by CTCA. A combined assessment of coronary anatomy and
45 function is therefore desirable, but it generally requires two separate diagnostic tests resulting in
46 higher immediate costs. Accordingly, although the advantages of a comprehensive anatomo-
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6 functional evaluation of patients with suspected ischemic heart disease have been confirmed [37,
7 38], such an integrated assessment is rarely performed in daily routine.

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9 While CTCA has long represented the reference standard for the non-invasive depiction of
10 coronary anatomy, more recently it is also being used to obtain quantitative measures of CAD
11 functional relevance through the modelization of coronary flow dynamics [7, 39]. The calculation
12 of FFR_{CT}, the most validated of such functional parameters, typically requires the use of proprietary
13 software with long computation times and a dedicated core-laboratory [17, 33]. Our results suggest
14 that vFAI might represent a valid alternative to the more technically demanding FFR_{CT}, allowing
15 a close estimation of invasive FFR and discriminating hemodynamically significant coronary
16 lesions with good accuracy. The required analysis time was around 25 minutes that is significantly
17 lower when compared to that of the most well-known FFR_{CT} software (1-4 hours) [8] and is directly
18 comparable to that of the study by Kruk *et al.* (average of 20 minutes per case) [9], or of the study
19 by Ko *et al.* (average of 27 minutes per case) [13]. Moreover, the proposed method requires
20 minimal user interaction regarding the 3D reconstruction process of the desired arterial segment,
21 resulting in a good interobserver as well as intraobserver agreement.
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31 32 33 **Study Limitations**

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35 We have performed a retrospective analysis in a rather modest sample size. On the other hand, in
36 contrast to most previous studies, we have evaluated only patients with intermediate likelihood of
37 CAD. In this group that is of particular clinical relevance, we have demonstrated good agreement
38 between vFAI and FFR and our results compare well with prior studies on CTCA based
39 modellization of coronary flow dynamics. We acknowledge that for the time being, our method
40 can only perform a vessel-based reconstruction and not that of the entire arterial tree. Nevertheless,
41 for the purposes of the current study this was not a drawback, since we only assessed specific
42 segments on which FFR was invasively measured. We are currently improving the algorithm to
43 have the ability to perform a full 3D reconstruction of the entire arterial tree and this will be tested
44 in a larger prospective study aiming to include also individuals with clinical characteristics broader
45 than those described in the current study. Finally, striving for an almost absolute agreement
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between vFAI and FFR is probably an elusive task considering the intrinsic nature of vFAI. The latter mainly expresses the "potential" functional impact of anatomy, which differs fundamentally from the invasively calculated FFR that measures directly the effect of anatomy on real pathophysiologic conditions and thus, may be influenced by the vasodilating capability of the whole coronary system.

CONCLUSIONS

vFAI can be effectively derived from the application of CFD to three-dimensional CTCA datasets with a consistently limited computation effort. In patients with coronary stenoses 30-90%, vFAI performs well against the invasive gold standard represented by FFR and can distinguish hemodynamically significant from non-significant coronary lesions.

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Figure Legends

Fig. 1: A) 3D Reconstruction Process Flowchart. B) Reconstruction process. The orange arrow indicates the point of the RCA that was annotated by the user. C) 3D reconstructed artery, which is derived from the previously annotated point. D) Pressure distribution for flow rates of 1 ml/s and 3 ml/s. Red color indicates a pressure of 100 mmHg whereas the deep blue color indicates a pressure value of 88 mmHg. E) Invasively measured FFR was 0.92, the same as the respective vFAI.

Fig.2: Examples of ischemic cases. A) Pressure distribution in RCA with an invasively measured FFR of 0.66 and a vFAI of 0.64. B) Pressure distribution in LAD with an invasively measured FFR of 0.79 and a vFAI of 0.82.

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Fig.23: A) Regression plot comparing the two methods. B) Bland-Altman plot comparing the two methods.

Fig.34: ROC curves comparing vFAI vs. CTCA diagnostic performance to recognize hemodynamically significant coronary lesions ($FFR \leq 0.80$). The area under the curve (AUC) for the vFAI is 0.97 (95% CI: 0.90-0.99, $P < 0.0001$), whereas for CTCA is 0.56 (95% CI: 0.44-0.68, $P = 0.297$).

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whereas for CTCA is 0.62 (95% CI: 0.5-0.73, $P = 0.096$).

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Table Legends

Table 1. Baseline Characteristics of the study population (N=63)

Table 2: Per-vessel Diagnostic performance for vFAI and CTCA

Table 1

Cardiovascular Risk Factors

Age	62.9 (\pm 7.8)
BMI, kg/m ²	27.8 (\pm 4.9)
Body Mass, kg	81 (\pm 15.8)
Diabetes (N, %)	14 (22.2%)
Smoker during past year (N, %)	16 (25.4%)
Hypertension (N, %)	41 (65%)
Hypercholesterolemia (N, %)	42 (66.7%)
CT Coronary Calcium Score –Agatston (N, %)	
CAC = 0	6 (9.5%)
CAC = 1 – 99	13 (20.6%)
CAC = 100 – 399	21 (33.3%)
CAC \geq 400	19 (30.2%)
CAC Not done	4 (6.3%)
Obstructive CAD (N, %)	
Obstructive CAD at CTCA (> 50% stenosis)	39 (61.9%)
Obstructive CAD at ICA (> 50% stenosis)	35 (55.6%)

Table 2

FFR \leq 0.80

	Accuracy (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	TP	TN	FP	FN
vFAI \leq 0.82	93.2	87.5	96	91.3	94.1	21	48	2	3
CTCA Stenosis \geq50%	52.7	66.7	46	37.2	74.2	16	23	27	8

FFR $<$ 0.80

	Accuracy (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	TP	TN	FP	FN
vFAI \leq 0.82	96	95.5	96.2	91.3	98	21	50	2	1
CTCA Stenosis \geq50%	51.4	66.7	45.3	32.6	77.4	14	24	29	7







