**Benha Journal of Applied Sciences (BJAS)** **print: ISSN 2356–9751**
**Vol. (7) Issue (8) (2022), (11-16)** **online: ISSN 2356–976x**

**http://bjas.journals.ekb.eg**

# Diagnostic value of coronary computed tomography angiography in comparison with invasive coronary angiography and FFR in patients with intermediate and severe coronary artery stenosis

**E.M.Ghareeb, H.M.Abuelenin, M.A.Salem and M.M.Ali**
Cardiology, Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-mail: Ahmed989@icloud.com

**Abstract**

Background: The presence of myocardial ischemia is an important risk factor for an adverse clinical outcome. Revascularizations of stenotic coronary lesions that induce ischemia can improve a patient's functional status. The aim of the present study was to evaluate the diagnostic accuracy of CT coronary angiography in patients with moderate to severe coronary artery lesions in correlation with invasive coronary angiography and fractional flow Reserve (FFR). Methods: The current study was a prospective analysis of 70 individuals who had coronary computed tomography angiography (CCTA), diameter stenosis was calculated. Then, patients were divided into two groups according to CCTA results, either intermediate coronary artery stenosis (50% to 69% diameter stenosis) or severe coronary artery stenosis (≥ 70% diameter stenosis), and the two groups referred to invasive coronary angiography and distal pressure and aortic pressure were measured and FFR was calculated. This study took place in Mediclinic Al Ain Hospital, Mediclinic Al Madar Medical Center, Al Madar diagnostic center and Medical Heart Center in Al Ain city, United Arab Emirates. Results: Out of 70 patients, 36 (51.4%) underwent PCI to LAD, 13 (18.6%) underwent PCI to LCX, 7 (10%) underwent PCI to RCA and 16 (22.9%) weren't subjected to any procedure. Stenosis in different vessels (LAD, LCX and RCA) was evaluated by CT angiography and invasive coronary angiography, by comparing between the two methods, the stenosis was found insignificantly different. The mean difference in LAD stenosis was 1.6 ± 12.67 (limits of agreement -23.2: 26.4), was -1.4 ± 13.56 (limits of agreement -27.9: 25.2) in LCX and was 3.1 ± 7.51 (limits of agreement -11.6: 17.8) in RCA. The ability of CT angiography and FFR in evaluating the significance of stenosis was comparable. The ability of invasive coronary angiography and FFR in evaluating the significance of stenosis was comparable. Conclusion: In CAD patients with artery stenosis, the stenosis in different vessels (LAD, LCX and RCA) was evaluated by CT angiography, invasive coronary angiography and fractional flow reserve that were insignificantly different. Thus, developing non- invasive methods for evaluation of stenosis is important for practitioners in determining individuals at high risk for advanced ischemia heart disease who might need a more aggressive therapeutic approach and closer clinical follow-up.

**Key words:** coronary computed tomography angiography, Diagnostic value, invasive coronary angiography, coronary artery stenosis, fractional flow Reserve, FFR**.**

## 1. Introduction

The presence of myocardial ischemia is an important risk factor for an adverse clinical outcome. [1-3] Revascularizations of stenotic coronary lesions that induce ischemia can improve a patient's functional status and outcome. [3-5] For stenotic lesions that do not induce ischemia, however, the benefit of revascularization is less clear, and medical therapy alone is likely to be equally effective.[6-7]

Coronary computed tomography angiography (CCTA) is a noninvasive and accurate diagnostic tool to detect coronary artery disease (CAD), and is increasingly utilized in clinical practice. Diagnostic accuracy of 64-multidetector row CCTA has been validated in several multicenter trials, and the high negative predictive value establishes CCTA as an effective noninvasive alternative to invasive coronary angiography to rule out obstructive coronary artery stenosis.[8-9] However, the diagnosis of CAD stenosis by CCTA demonstrates an unreliable accuracy to define the lesion-specific ischemia.[10] With a concern that widespread use of CCTA may result in excess referral of patients to invasive coronary angiography and unnecessary revascularization of non-ischemic coronary lesions, several methods were developed and suggested to have the ability to evaluate for both anatomical and functional stenosis. [11–13]

At present, the gold standard assessment of the hemodynamic significance of coronary stenosis is fractional flow reserve (FFR). It is defined as the ratio of maximal blood flow in a stenotic artery to normal maximal flow. [14] It can be easily measured during coronary angiography by calculating the ratio of distal coronary pressure measured with a coronary pressure guidewire to aortic pressure measured simultaneously with the guiding catheter. FFR in a normal coronary artery equals 1.0. An FFR value of 0.80 or less identifies ischemia-causing coronary stenosis with an accuracy of more than 90%. [14-16]

Deferring PCI in non-ischemic stenotic lesions as assessed by FFR is associated with an annual rate of death or myocardial infarction of approximately 1% in patients with single-vessel coronary artery disease, which is lower than the rate after routine stenting. [7] On the other hand, deferring PCI in lesions with an FFR of less than 0.80 may result in worse outcomes than those obtained with revascularization. [17]

The aim of this work was to evaluate the diagnostic accuracy of CT. coronary angiography in patients with moderate to severe coronary artery lesions in correlation with invasive coronary angiography and fractional flow Reserve (FFR).

## 2. Patients and Methods

This study was conducted on 70 adult patients who presented with anginal chest pain and had intermediate pretest probability for coronary artery disease (CAD) and was admitted at Medicine Al Ain Hospital, Mediclinic Al Madar Medical Center, Al Madar diagnostic center and Medical Heart Center in Al Ain city, United Arab Emirates. Treadmill exercise test was done to all patients for risk stratification.

All the patients assessed by coronary computed tomography angiography (CCTA) with the Exclusion criteria included:

- Atrial fibrillation.
- High-grade atrioventricular block.
- Renal insufficiency (estimated glomerular filtration rate $\leq$ 60 ml/min/1.73 $m^2$).
- Broncho spastic lung disease requiring long-term steroid therapy.
- Morbid obesity (body mass index $\geq$ 40 $kg/m^2$).
- Allergy to iodinated contrast.
- Patients with left main (LM) disease.

The location and extent of the coronary lesion was manually assigned, and the diameter stenosis was calculated.

These patients were divided into two groups according to CCTA results, either intermediate coronary artery stenosis (50% to 69% diameter stenosis) or severe coronary artery stenosis ($\geq$ 70% diameter stenosis), and the two groups were referred to invasive coronary angiography which was done using standard techniques and projections and FFR was measured for all patients.

The pressure was measured just distally to the lesion during maximal hyperemia, Aortic pressure was measured through the guide catheter, and FFR was calculated as the ratio between mean distal pressure and mean aortic pressure. An FFR $\leq$ 0.80 considered functionally significant.

### Statistics

Results will be organized, tabulated and statistically analyzed using statistical package for social science (SPSS). For quantitative data, the mean and standard deviation will be calculated; the difference between two means will be statistically analyzed using the student (t) test.

For qualitative data, the number and percent distribution will be calculated. Chi square test will be used as a test of significance and when found inappropriate fisher exact test will be used significant and will be adapted to P-values < 0.05 for interpretation of statistically significant results.

**1- Mean value**

**2- Standard Deviation [SD]:**

**3- Standard student "t test"**

The calculated "t" was compared with tabulated one at different levels of significance at the degree of freedom (DF):

**4- Chi-square** the hypothesis that the row and column variables are independent, without indicating strength or direction of the relationship. Pearson chi-square and likelihood-ratio chi-square. Fisher's exact test and Yates' corrected chi-square are computed for 2x2 tables. **Chi-square test:** For comparison between two groups as regards qualitative data.

## 3.Results

**Table (1)** Treadmill test and procedure performed in the studied patients.

| | | n =70 |
|---|---|---|
| **TMT** | **Positive** | 52 (74.3%) |
| | **Negative** | 18 (25.7%) |
| **Procedure** | **PCI to LAD** | 36 (51.4%) |
| | **PCI to LCX** | 13 (18.6%) |
| | **PCI to RCA** | 7 (10%) |
| | **None** | 16 (22.9%) |

TMT: treadmill test, PCI: percutaneous coronary intervention, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: Right coronary artery

Regarding TMT, 52 (74.3%) patients were positive and 18 (25.7%) were negative.

Out of 70 patients, Thirty six patients (51.4%) underwent PCI to LAD, Thirteen patients (18.6%) underwent PCI to LCX, Seven patients (10%) underwent PCI to RCA and 16 (22.9%) weren't subjected to any procedure. **[Table 1]**

**Table (2)** Comparison between coronary CT angiography and invasive coronary angiography in evaluation of stenosis in the studied patients**.**

| | | CT angiography | Invasive coronary angiography | P value |
|---|---|---|---|---|
| **LAD (%)** | **Mean ± SD** | 69 ± 11.11 | 67.4 ± 13.37 | 0.517 |
| | **Range** | 40 - 90 | 40 - 90 | |
| | **Moderate stenosis** | 12 (17.1%) | 16 (22.9%) | 0.378 |
| | **Severe stenosis** | 38 (54.3%) | 34 (48.6%) | |
| **LCX (%)** | **Mean ± SD** | 63.48 ± 13.69 | 66.36 ± 17.61 | 0.542 |

| | | | | |
|---|---|---|---|---|
| | **Range** | 30 - 80 | 30 - 90 | |
| | **Moderate stenosis** | 8 (11.4%) | 8 (11.4%) | |
| | **Severe stenosis** | 15 (21.4%) | 14 (20%) | 0.912 |
| | **Mean ± SD** | 60 ± 15.12 | 59.23 ± 16.56 | 0.899 |
| | **Range** | 30 - 80 | 30 – 80 | |
| **RCA (%)** | **Moderate stenosis** | 6 (8.6%) | 5 (7.1%) | |
| | **Severe stenosis** | 9 (12.9%) | 8 (11.4%) | 0.934 |

LAD: left anterior descending artery, LCX: left circumflex artery, RCA: Right coronary artery
Stenosis in different vessels (LAD, LCX and RCA) was evaluated by CT angiography and Invasive coronary angiography, by comparing between the two methods, the stenosis was found insignificantly different. **[ Table 2]**

**Table (3)** Agreement between CT angiography and invasive coronary angiography in evaluation of stenosis calculated by Bland Altman analysis (n=70)

| | **Mean** | **SD** | **Lower limit of agreement** | **Upper limit of agreement** |
|---|---|---|---|---|
| **LAD (%)** | 1.6 | 12.67 | -23.2 | 26.4 |
| **LCX (%)** | -1.4 | 13.56 | -27.9 | 25.2 |
| **RCA (%)** | 3.1 | 7.51 | -11.6 | 17.8 |

The mean difference in LAD stenosis was 1.6 ± 12.67 (limits of agreement -23.2: 26.4), was -1.4 ± 15.52 (limits of agreement -31.8: 29.1) in LCX and was 3.1 ± 7.51 (limits of agreement -11.6: 17.8) in RCA. **[ Table 3]**

**Table (4)** The degree of stenosis evaluated by CT angiography and FFR in the studied patients (n=70)

| | | **CT angiography** | **FFR** | **P value** |
|---|---|---|---|---|
| **LAD** | **Significant >70%** | 38 (54.3%) | 35 (50%) | 0.331 |
| | **Insignificant <70%** | 12 (17.1%) | 17 (24.3%) | |
| **LCX** | **Significant >70%** | 15 (21.4%) | 11 (15.7%) | 0.787 |
| | **Insignificant <70%** | 8 (11.4%) | 7 (10%) | |
| **RCA** | **Significant >70%** | 9 (12.9%) | 8 (11.4%) | 1.00 |
| | **Insignificant <70%** | 6 (8.6%) | 4 (5.7%) | |

FFR: fractional flow reserve, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: Right coronary artery
The ability of CT angiography and FFR in evaluating the significance of stenosis was comparable.
Table (4)

**4. Discussion**

In the present study, regarding the treadmill test (TMT) and procedure performed for the study participants, regarding TMT, 52 (74.3%) patients were positive and 18 (25.7%) were negative.

Comparable to our results, Ramaiah et al., [18] who showed that among patients with FFR < 0.75, TMT was done and revealed that 80% of patients were positive and 20% were negative for inducible ischemia. In seven patients with an FFR of >0.75 TMT was done in 6 patients, 3(50%) were positive and 3(50%) were negative for inducible ischemia.

Moreover, 36 (51.4%) underwent PCI to LAD, 13 (18.6%) underwent PCI to LCX, 7 (10%) underwent PCI to RCA and 16 (22.9%) weren't subjected to any procedure.

Guelker et al., [19] concluded a contradictory results in the study conducted to identify patients who underwent PCI supported by a GL GuideLiner® (GL) catheter (Vascular Solutions Inc.) in CAD patients. The results showed that PCI was highest in the RCA followed by the LAD and LCX at 53%, 22% and 17%, respectively. Different sample size, study design and different population could explain these conflicted results.

Further, Reczuch et al., [20] who enrolled 16 patients with stable angina (11 males, mean age 60±9 years) with 34 lesions localised in the main epicardial coronary arteries [LAD / LM / RCA/ intermediate branch (IB) / LCx] to assess long-term outcome in patients with multi-vessel CAD and borderline lesions, including LAD, in whom fractional flow reserve (FFR) in all affected vessels was measured and used for selection for PCI or conservative treatment. The results explained that in (23%) of participants the FFR value was <0.75 and these lesions were treated with PCI (37.5%) in patients with

LAD stenosis, (37.5%) in patients with LCX and 25% for other lesions.

The present study conducted a comparison between coronary CT angiography and invasive coronary angiography for evaluation of stenosis in different vessels (LAD, LCX and RCA) and showed that: stenosis by CT angiography was moderate in 6 patients (8.5%), while it was severe stenosis by invasive angiography, and CT angiography showed severe stenosis in 10 patients (14.2 %) while it was moderate stenosis by invasive angiography : so both methods was insignificantly different in evaluation of coronary arteries stenosis.

In agreement with our results, Elagha et al., [21] conducted their prospective study on 50 patients undergoing a routine cardiac catheterization for preoperative evaluation of CAD. The results showed that the coronary computed tomography angiography (CCTA) could exclude with confidence the presence of RCA, and LCX significant stenosis among the rest of the patients with 100% diagnostic accuracy. Although there was a little decrease in diagnostic accuracy of CCTA compared to the invasive conventional coronary angiography (CAG) regarding the diagnosis of significant stenosis in LAD vessel, however, it reaches 95.7%, which still represents a high level of diagnostic accuracy.

The published ACC/AHA guidelines 2014 stated that CCTA is reasonable to exclude the presence of significant obstructive CAD in selected patients with a low/ intermediate pretest probability of CAD, while a positive CCTA is to be confirmed with invasive CAG. [22]

Moreover, Elagha et al., [21] showed a high degree of accuracy of how CCTA could determine the presence of CAD and significant coronary stenosis (≥ 50%).

Similar to our findings, Sun et al., [23] described a direct comparison of CCTA and conventional invasive coronary angiography for 51 patients to detect coronary artery stenosis in CAD patients and demonstrates that CCTA can provide diagnostic accuracy in detecting significant CAD and are reliable for excluding significant CAD, without significant differences on a vessel- or a patient-based level. The results showed that for all vessels, CCTA like CAG demonstrated high image quality to detect significant stenosis in a patient-, and vessel-based analysis.

These study results are consistent with Pouleur et al., [24] who evaluated the diagnostic accuracy of CCTA on each vessel-based assessment to detect coronary disease in patients prior to cardiac valve surgery. The per-vessel analysis for 82 patients by CCTA showed significantly higher accuracy for the left main (99%) followed by RCA (93%) then LCX (91%) while the lower accuracy was in LAD (88%), which nearly agrees with our results.

In our study, the agreement between CT angiography and invasive coronary angiography in evaluation of stenosis calculated by Bland Altman analysis and revealed that the mean difference in LAD stenosis was 1.6 ± 12.67 (limits of agreement -23.2: 26.4), was -1.4 ± 13.56 (limits of agreement -27.9: 25.2) in LCX and was 3.1 ± 7.51 (limits of agreement -11.6: 17.8) in RCA.

Further, Renker et al., [25] conducted a post hoc sub study on 330 patients (75.2% male, median age 63 years) with coronary artery stenosis to investigate the influence of stenosis location in the coronary artery system on the performance of ML-CT-FFR in a large, multicenter cohort. The study conducted a Bland-Altman analyses comparing CCTA and invasive CT angiography and showed that 0.05 (limits of agreement: 0.32 to 0.21) in the RCA, -0.02 (-0.27 to 0.22) in the LAD, -0.03 (0.26 to 0.20) in the LCX.

The present study evaluated the degree of stenosis evaluated by CT angiography and FFR in the studied patients and observed that the ability of CT angiography and FFR in evaluating the significance of stenosis was comparable.

Additionally, our findings evaluated the degree of stenosis by invasive coronary angiography and FFR in the studied patients and showed that the ability of invasive coronary angiography and FFR in evaluating the significance of stenosis was comparable.

Our results are harmonious with Wardziak et al., [26] who carried out their study on 96 intermediate stenosis (50–90%) from 90 subjects, with intermediate pre-test probability of CAD, who underwent coronary CTA. The results showed that identification of significant stenosis evaluated by invasive routine coronary angiography did not significantly differ compared to FFR.

In accordance with our results, Gonzalez et al., [27] performed a meta-analysis study to compare the diagnostic performance of CCTA, computed tomography perfusion (CTP), and computed tomography (CT)-fractional flow reserve (FFR) for assessing the functional significance of coronary stenosis as defined by invasive FFR in CAD patients. They found that CT angiography and FFR had similar sensitivity in evaluating the stenosis.

Contrasted to our results, Renker et al., [28] who measured CT-based FFR in 67 coronary lesions from 53 individuals in a blinded method. The pressure guidewire-based FFR of 0.80 was used as the reference standard to identify hemodynamically significant stenosis and to compare the diagnostic efficacy of CT-based FFR to routine CCTA assessment (luminal diameter stenosis of 50%). The results revealed that the hemodynamically significant stenosis can be detected on-site using FFR method, which performs better than the usual CCTA assessment. Certain differences in study design and patient characteristics could be considered for the discrepant results.

In contrary, Voros et al., [29] reported an improved diagnostic performance of quantitative anatomic CCTA measurements over visual stenosis grading in correlation with FFR. This could be explained by an important difference, Voros et al., study included intermediate and severe lesions. This has introduced a bias in which even the most severe lesions could be interrogated by CTA, thus increasing its performance. Moreover, they used a per-lesion analysis, in which a prespecified lesion was interrogated with all 4 modalities in addition to using a fully quantitative, 3-dimensional analysis of the entire vessel segment.

## 5. Conclusion

In CAD patients with artery stenosis, the stenosis in different vessels (LAD, LCX and RCA) was evaluated by CT angiography, invasive coronary angiography and fractional flow reserve that were insignificantly different. Thus, developing non- invasive methods for evaluation of stenosis is important for practitioners in determining individuals at high risk for advanced ischemia heart disease who might need a more aggressive therapeutic approach and closer clinical follow-up.

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