The Impact of Atrial Fibrillation on Quantitative Flow Ratio Measurements in Patients With Coronary Artery Disease

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Abstract

Quantitative Flow Ratio (QFR) is now a new method for the assessment of the extent of coronary artery stenosis but may be obscured by involvement of the mutated status of anatomical structure and blood flow in the coronary artery when encountering Atrial Fibrillation (AF). In this study, we aimed to expose the effect of mutated status of anatomical structure and blood flow on QFR results in AF patients.

Methods and results: We evaluated QFR on 223 patients (112 patients with AF; 111non-AF patients served as control) who had undergone PCI-ES due to severe stenoses in coronary arteries. QFR of the target coronary was determined according to the flow rate of the contrast agent, results showed that AF patients with significantly higher QFR value than control group (0.792 ± 0.011 vs. 0.685 ± 0.016, p□0.001). Then we further analyzed the local QFR around the stenoses (0.858 ± 0.0287 vs. 0.756 ± 0.014, p=0.002), residual QFR (0.958 ± 0.005 vs. 0.929 ± 0.009, p=0.005), index QFR (0.807 ± 0.010vs. 0.713 ± 0.014, p<0.0001) in these two groups of patients with and without AF. Further analysis revealed that AF patients accompanied with relatively lower blood flow velocity (0.130 ± 0.006 m/s vs. 0.153 ± 0.005 m/s, p=0.003) in the diseased coronary artery as compared to the control. Meanwhile we observed that AF patients with higher minimum lumen area (MLA, mm^2) (1.65 ± 0.097 vs. 1.11 ± 0.062, p□0.001) and decreased maximum lesion distorted angle (28.14°± 1.16°vs. 31.95°± 1.23°, p=0.025) compared to the control.

Conclusion: Mutated status of anatomical structure and blood flow in the coronary artery of AF patients may enlarge the value of QFR, this may be ascribed to the lower blood flow velocity and decreased maximum lesion distorted angle in AF patients.

Introduction

Fractional flow reserve (FFR) is accepted as the gold standard for the diagnosis of intracoronary insufficiency significance when stenosis. However, on one hand, due to the invasiveness and complexity of the operation as well as the side effects of drugs such as adenosine or ATP using in the operation leading to the limitations of clinical application of FFR. On the other hand, the high cost of pressure guide wires also greatly limited the clinical application of FFR especially in developing countries.

Recently, image based non-invasive QFR computing technology has emerged as a hot technology in the international cardiovascular field in the catheterization laboratory [1]. Clinical investigation has shown that QFR can greatly simplify the assessment process of FFR, without using invasive pressure guide wire and also can achieve higher diagnostic accuracy without using vasodilator drugs of microcirculation. The diagnostic sensitivity and specificity of QFR were significantly better than quantitative coronary angiography [2]. The results of QFR suggested that patients with lesions of QFR < 0.80 had a higher risk of adverse events. Besides, QFR has been written into the expert consensus in the field of acute myocardial infarction intervention in several countries [3-4]. QFR has now becoming a new tool in the catheterization room and provide guidance for clinicians to formulate interventional treatment strategies.

However, QFR still has a limitation in evaluating the functional significance of certain coronary stenosis especially endothelial dysfunction caused by atherosclerotic coronary artery disease or mutated status of blood flow such as in AF patients [5-6]. These limitations might cause an unnecessary myocardial revascularization. In this study, we aimed to investigate the possible effect of the mutated status of blood flow and anatomical structure in AF patients on QFR ratio results.

Methods

Inclusion and Exclusion criteria for patients

The patients who were involved were less than 80 years old and were admitted to Cardiac Center of Zhongda Hospital affiliated to Southeast All the patients were implanted with drugs-eluting stents in the coronary artery from 2014 to 2019. The inclusion criteria were as follows: (1) men or nonpregnant women ≥ 18 and ≤ 80 years of age; (2) AF patients with CHA_2DS_2-VASc score ≥ 2 and received coronary stent implantation; Control group were non-AF patients with received coronary stent implantation. This program was approved by the Ethical Committee of the Zhongda Hospital affiliated to Southeast University, China. Subjects showing any of the following exclusion criteria were not allowed to participate in the study: ≥ 80 years old or < 18 years old; eGFR (estimated glomerular filtration rate) of < 30 mL/ (minute•1.73 m^2); hemodynamic or electrical instability (including shock); and a platelet count of less than 90 × 10^9/L or hemoglobin less than 90 g/L.

Study procedures

Clinical data collection

Researchers interviewed patients and reviewed their medical records to obtain information on patients' medical history. Data on disease history were collected from the medical charts. The basic characteristics of patients were acquired from clinical or biochemical tests, which included a history of cardiovascular or cerebrovascular diseases, smoking, drug intake, and blood pressure. QFR in the whole target coronary. local QFR around the stenoses, residual QFR after stent implantation, index QFR after 3D reconstruction (**Figure 1**) were calculated using Angio Plus system (Pulse Medical Imaging Technology Co., China) by an independent committee who were unaware of treatment allocations adjudicated and verified all QFR related values that required.

Definitions different types of QFR

QFR of the target coronary, Ratio of the pressure at the farthest end of the target vessel to the pressure at the beginning of the coronary artery in the aortic sinus，referred to Pd/Pa shown in **Figure 2A**; Local QFR around the stenoses, Ratio of the pressure at the distal lesion of the target vessel to that at the proximal lesion，referred to Pd/Pa shown in Figure 2B，Residual QFR, Ratio of distal lesion pressure to proximal lesion pressure after stent implantation in target vessels，referred to Pd/Pa shown in Figure 2C，Index QFR,

The ratio of the pressure at the distal lesion to the pressure at the proximal lesion after 3D reconstruction of target vessels referred to Pd/Pa shown in Figure 2D.

Statistical analysis

Data management and statistical analysis were performed using SAS software version 9.1 (SAS Institute, USA). $P < 0.05$ was considered statistically significant. Data are expressed as the means ± standard deviations. Intergroup comparison of continuous variables was performed using Student's t test. Categorical variables were compared using the χ^2 test. Kaplan–Meier survival curves were used to compare event-free survival (the first occurrence of the clinical events) between groups.

Results

Baseline characteristics of the patients

A total of 223 patients in our cardiac center were enrolled, which including 112 patients with AF and 111patients without AF who served as control. The mean age of the AF patients in the trial was 70.28 years old and 65.22 years old in the control group. 66.61% of patients in AF group and 57.14% in the control group were male patients. Clinical comorbidities, including hypertension, diabetes, and history of stroke/TIA, and New York Heart Association classification grading of cardiac function as well as eGFR between the 2 groups were shown in **Table 1**. Baseline procedural characteristics were all comparable shown in **Table 2**. including PCI-related vessel and periprocedural treatment.

QFR results

We found higher QFR ratio in AF patients as compared to patients in the control group (0.792 ± 0.011 vs. 0.685 ± 0.016, p 0.001) which determined in the whole diseased coronary artery (**Figure 3.**). In consistent with the result of the whole diseased coronary artery, local QFR around the stenoses (0.858 ± 0.0287 vs. 0.756 ± 0.014, p=0.002), residual QFR (0.958 ± 0.005 vs. 0.929 ± 0.009, p=0.005), index QFR (0.807 ± 0.010vs. 0.713 ± 0.014, p<0.0001) were all higher in AF patients as compared to the control. These findings support the hypothesis that deduced from the FFR measurement [7-8].

QFR results of the corresponding coronary artery

We found a statistically significant difference in QFR results between patients had AF and did not have AF at the average level of all coronary arteries. Then we sought to distinguish whether these difference were donated by certain coronary arteries, We then compared the QFR values of Left anterior descending coronary artery (LAD), Left circumflex coronary artery (LCX), Right coronary artery(RCA) and other diseased vessels in the two groups. Results showed higher QFR ratio in LAD (0.781 ± 0.016 vs. 0.656 ± 0.020, p 0.001) and RCA as well as other vessels (0.801 ± 0.020 vs. 0.699 ± 0.053, p=0.045). QFR values of LCX showed comparable results (0.814 ± 0.024 vs. 0.751 ± 0.026, p=0.112) between AF patients and non-AF patients in the control group.

Flow resistance of the related coronary artery and blood flow velocity

After determined the QFR results, we sought to evaluate the relationship between extent and vascular resistance(mmHg*S/m) of the related coronary artery and blood flow velocity(M/s) on QFR results in AF patients. Then we found a lower trend of vascular resistance of the related coronary artery in AF patients as compared to the non-AF patients, however the result did not show significance （165.9 ± 11.51 vs. 199.9 ± 13.94，p=0.061）. It's worth noting that we revealed that AF patients with lower blood flow velocity as compared to the control group of non-AF patients (0.130 ± 0.006 vs. 0.153 ± 0.005, p=0.003). The above result implies that lower blood flow velocity might associated with an increased prevalence of QFR results in AF vessels.

Anatomy of the lesion

After determined the relationship between flow velocity and QFR results in AF patients, we next sought to evaluate whether the anatomy of the lesion could affect the results above. First, we found a comparable length of lesion(mm) in two groups of patients (18.83 ± 0.93 vs. 20.11 ± 0.92, p=0.328). However, results showed that the area rate (%) of stenosis at the lesion were significantly lower in AF patients (71.67 ± 1.291vs.77.6 ± 1.184, p=0.001). Consistent with the rate of lumen stenosis, AF patients showed higher minimum lumen area (MLA, mm^2) as compared to the control (1.65 ± 0.097 vs. 1.11 ± 0.062, p＜0.001). We further analyzed the mean distorted angle of the coronary(17.47°± 0.55°vs. 18.63°± 0.63°, p=0.167) and mean distorted angle of the lesion around the stenosis(17.36°± 0.74°vs.18.71°± 0.71°, p=0.189), both showed no significance. However, It's worth noting that AF patients showed a decreased maximum lesion distorted angle compared to the control(28.14°± 1.16°vs. 31.95°± 1.23°, p=0.025).

Discussion

The main objective of the current research was to compare the effect of a different blood flow status and anatomical characteristics on the QFR results of AF patients. Different from non-AF patients, AF patients might have certain changes of hemodynamic parameters and anatomical features such as lesion distorted angle. We observed that among patients with AF resulted in higher QFR results compared with non-AF patients. In addition, the comparison of local QFR, residual QFR, index QFR were all showed a significant difference between the 2 groups. Furthermore, Results also showed that AF patients accompanied with relatively lower resistance and lower blood flow velocity.

Unlike coronary angiography alone, recently, QFR has enabled interventional cardiologists more easily to accurately determine whether coronary atherosclerotic plaques are responsible for myocardial ischemia. Though FFR remains the gold standard for the detection of ischemia-inducing coronary stenoses, QFR through a computational fluid dynamic analysis, proved to be useful in discriminating functionally significant stenosis, which is an excellent correlation with FFR values[9] .QFR is an innovative angiographic-based technique that uses modern software for three-dimensional vessel reconstruction, and flow models calculation, which guided PCI not only has been also demonstrated superior to an

angiography-guided PCI and over medical therapy alone but also served as an modern, effective and usable tool now.

Despite the excellent correlation and agreement between QFR and FFR, there were discordance of functional ischemia between the 2 measures [10]. In accordance with our results, previous researchers had reported that the physiologic characteristics, such as microcirculation, might affect the diagnostic performance of QFR [11-12]. We here found that AF patients with lower trend of vascular resistance of the related coronary artery and lower blood flow velocity compared to the non-AF patients, which might imply that the coronary microcirculation has different characteristics in the two pathological populations. Given the fact that there might be lack of understanding regarding such discrepancies and their related factors, we sought to determine the difference of anatomy of the lesions in two groups. Then we found that AF patients with decreased maximum lesion distorted angle compared to the non-AF patients. Our results could offer an important insight into other studies that better understanding of these certain anatomies in AF patients may further improve the diagnostic accuracy of QFR analysis.

As we already known that QFR is computationally calculated, based on three dimensional QCA analysis from 2 different angiographic projections and is therefore directly affected by whether the target lesion is clearly visualized on CAG or not [13-14], as a result, the anterior descending coronary artery is susceptible to the overlap of the diagonal or septal branches, while the right coronary artery is susceptible to the curvature of the vessels. In order to get rid of these possible factors, we next compared the corresponding coronary artery of LAD, RCA and LCX in two groups, and further identified that AF patients still with higher QFR ratio in LAD and RCA as well as other vessels except for LCX. Except for anatomy and microcirculation between the groups the reasons of variances included there maybe the baseline variability of the patients and their myocardial mass for we did calculated that AF group patients with more incidence of stroke and cardiac insufficiency as shown in Table 2, in addition to this, AF patients in the trial showed decreased eGFR level as compared to the control, which might contribute the impair of myocardial resilience.

Conclusions

QFR has enabled interventional cardiologists more easily to accurately determine whether coronary atherosclerotic plaques are responsible for myocardial ischemia. However, patients with atrial fibrillation not only have more risk factors but also have specific coronary hemodynamic characteristics. The mutated status of anatomical structure and blood flow in the coronary artery of AF patients may enlarge the value of QFR, and this may be ascribed to the lower blood flow velocity and decreased maximum lesion distorted angle in AF patients. Better understanding of these certain anatomy and certain difference in AF patients may promote coronary interventionists further improve the diagnostic accuracy of QFR analysis.

Declarations

Sources of Funding

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Ethics approval

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration revised in 1975.

Competing interests

The authors hereby declare that no competing interests exist.

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Tables

Table 1. Characteristics of the Patients at Baseline

Characteristics	AF Patients (n = 112)	Control Group (n = 111)	*P* value
Age (years)	70.28 ± 7.42	68.22 ± 10.53	0.0721
Sex (male), N	69 (66.61%)	64 (57.14%)	0.4964
eGFR (mL/min)	67.85±20.26	94.75±29.40	0.0001
Smoke, N	39(34.82%)	36 (32.43%)	0.7058
Comorbidities			
Diabetes	39 (34.82%)	44 (39.64%)	0.4567
Hypertension	83 (74.11%)	86 (77.48%)	0.5569
stroke/TIA	35 (31.25%)	13 (11.71%)	0.0004
NYHA(III-IV)	35 (31.25%)	11 (9.91%)	0.0001
Serum lipid			
ox-LDL	2.53±0.74	2.51±0.97	0.8424
TG	1.57±0.96	1.80±0.99	0.0872

Data are expressed as the mean ± standard deviation and n (%).

NYHA, New York Heart Association classification grading of cardiac function; eGFR□estimate glomerular filtration rate□ox-LDL□oxidized low density lipoprotein□TG□triacylglycerol

Table 2. Baseline Procedural Characteristics

Characteristics	AF Patients (n = 112)	Control Group (n = 111)
ACS patients	17 (15.18%)	14 (12.16%)
Number of drugs-eluting stent		
1	96 (85.71%)	84 (75.68%)
2	16 (14.29%)	26 (23.42%)
≥3	0（0%）	1（0.90%）
PCI vessel		
LAD	61 (54.46%)	74 (66.67%)
LCX	18 (16.07%)	30 (27.03%)
RCA and other vessels	33 (29.46%)	7 (6.31%)
Periprocedural treatment		
Antiplatelet agent	112 (100%)	111 (100%)
GPIIbIIIa	20 (17.86%)	25 (22.52%)

Data are expressed as n (%). ACS, acute coronary syndrome; GPIIbIIIa, glycoprotein IIbIIIa receptor blocker; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main coronary artery; PCI, percutaneous coronary intervention; RCA, right coronary artery. Antiplatelet agent referred to Aspirin and clopidogrel or ticagrelor.

Figures

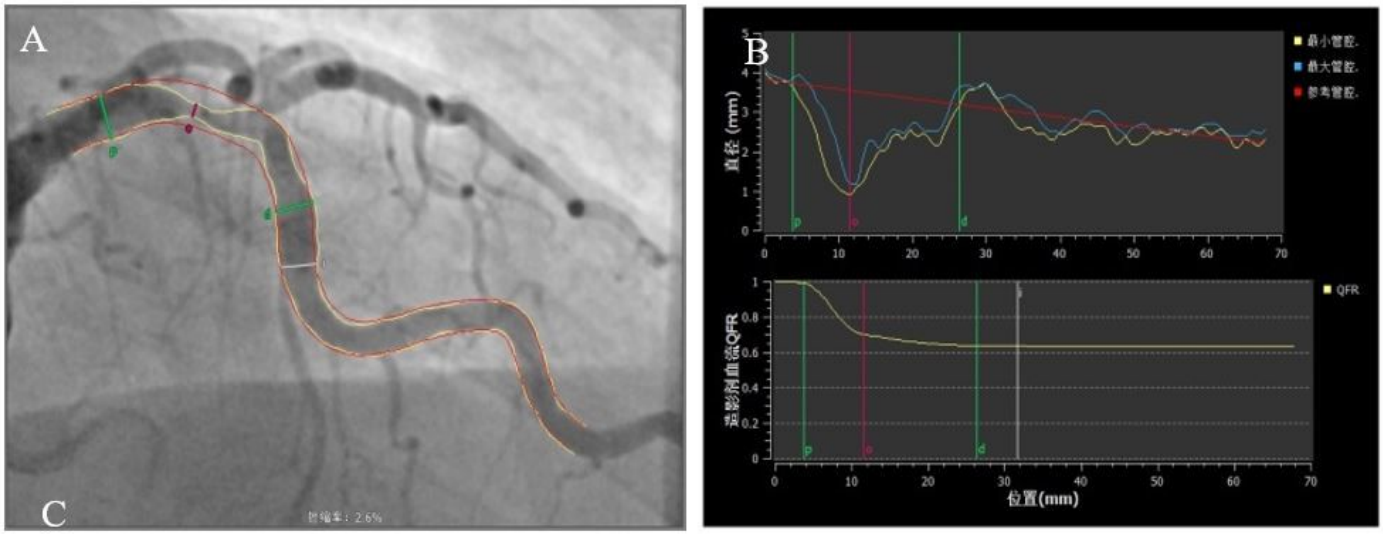

Figure 1

Schematic diagram of QFR measurement（A）Different sites of coronary artery lesions were selected as pressure detection points（B）The pressure values and overall curves of different sites of coronary artery lesions, Then QFR determined by Pd/Pa*100%.

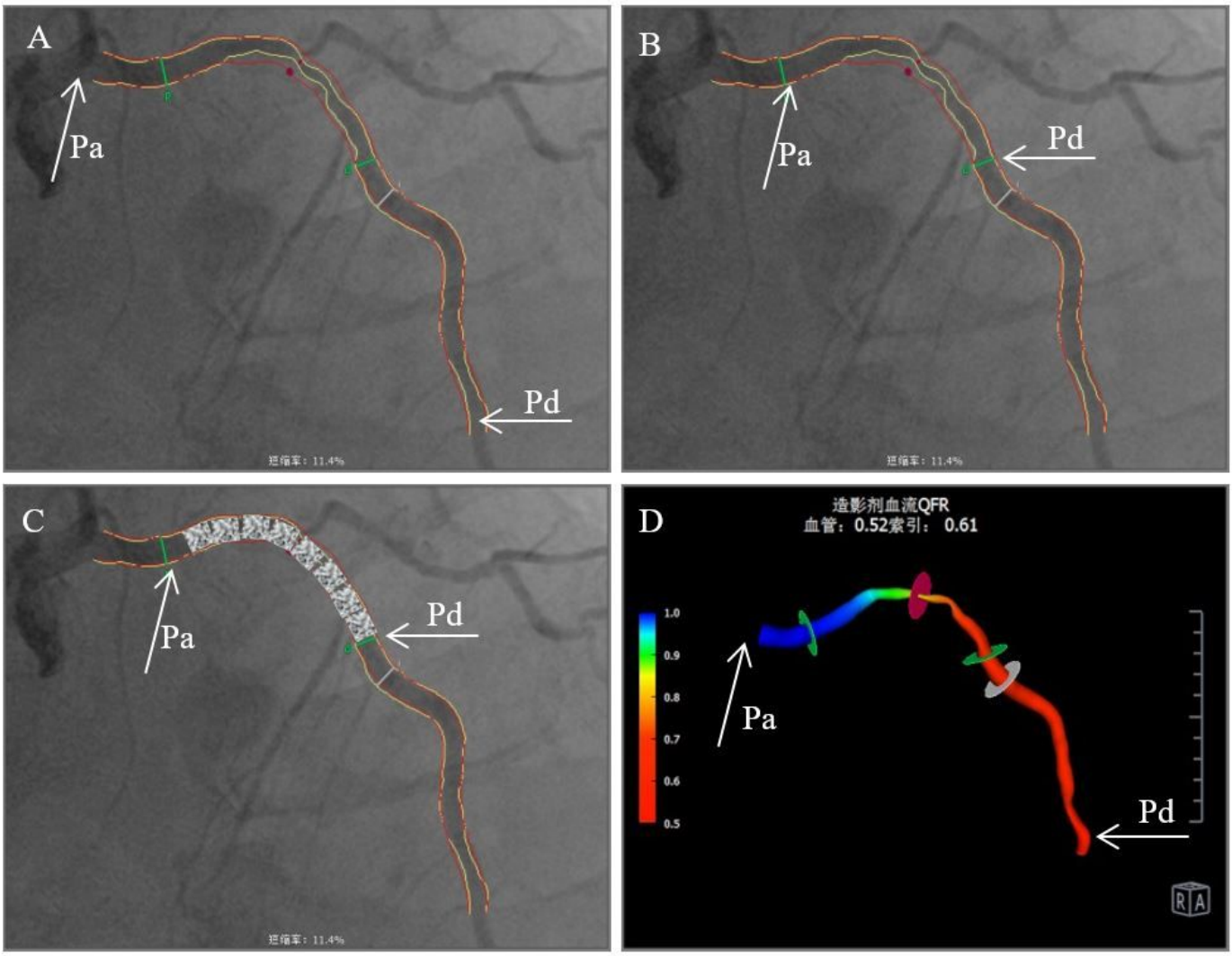

Figure 2

Differerent types of QFR were shown, A, QFR of the whole target coronary. B, local QFR around the stenoses, C, residual QFR after stent implantation, D, index QFR after 3D reconstruction.

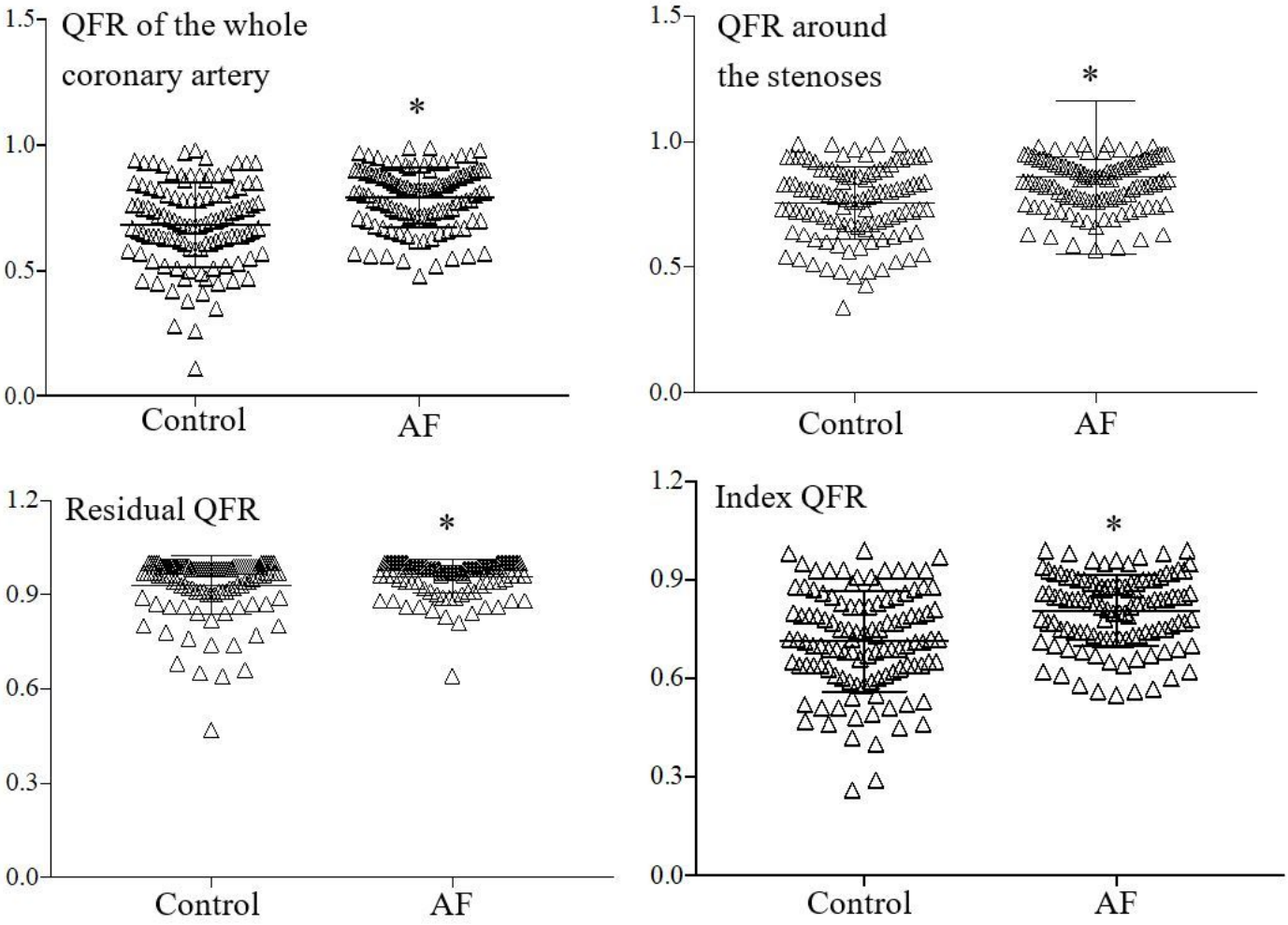

Figure 3

QFR ratio in AF patients and in the control group. QFR of the whole target coronary, local QFR, residual QFR, index QFR all higher in AF patients.

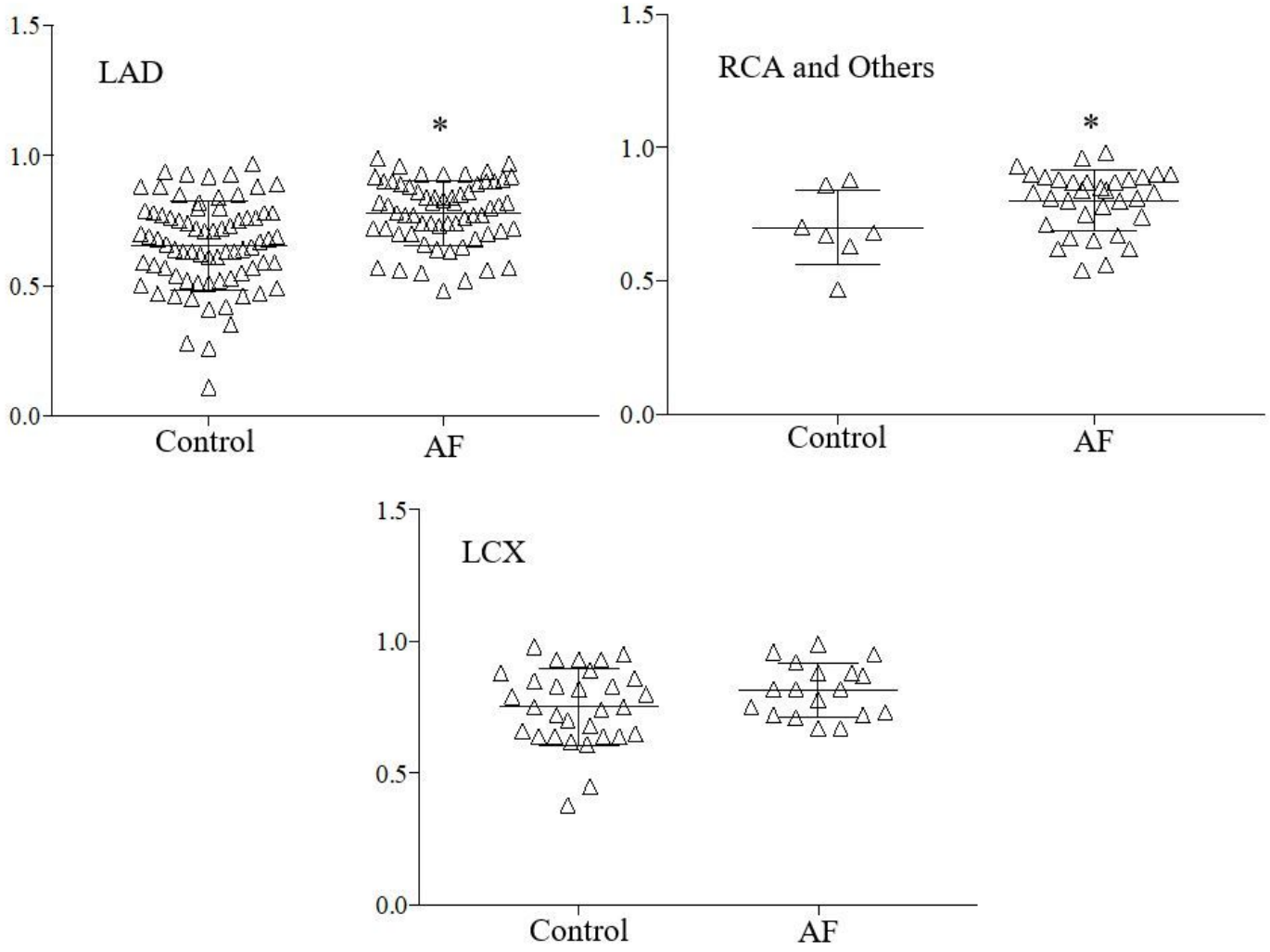

Figure 4

QFR results of the certain coronary artery in AF and control group. Higher QFR ratio were determined in LAD, RCA as well as other vessels as compared to control group.

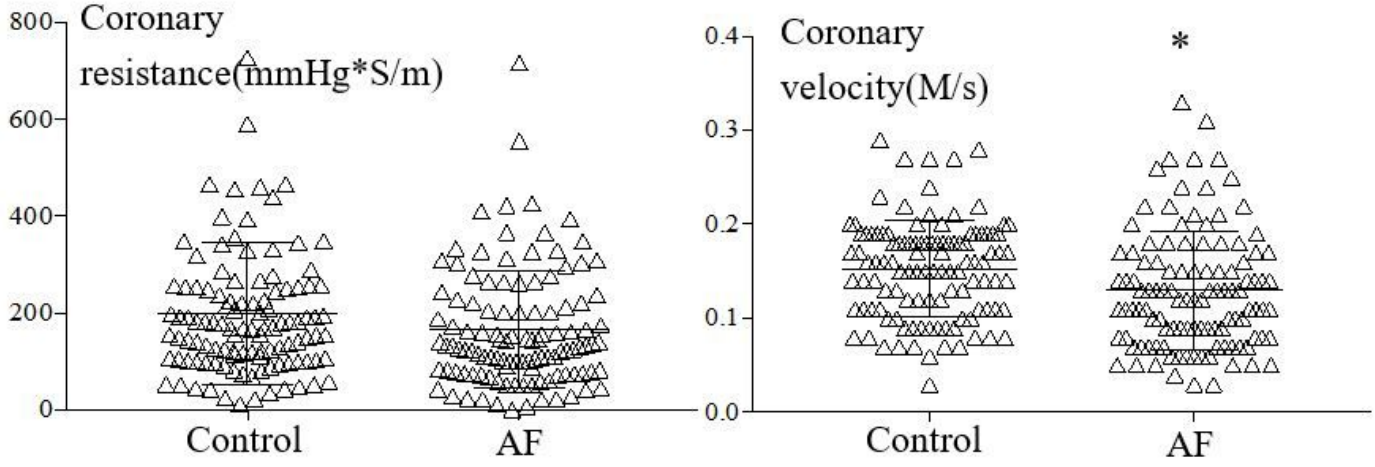

Figure 5

Flow resistance of the related coronary artery and blood flow velocity in AF patients and control group.

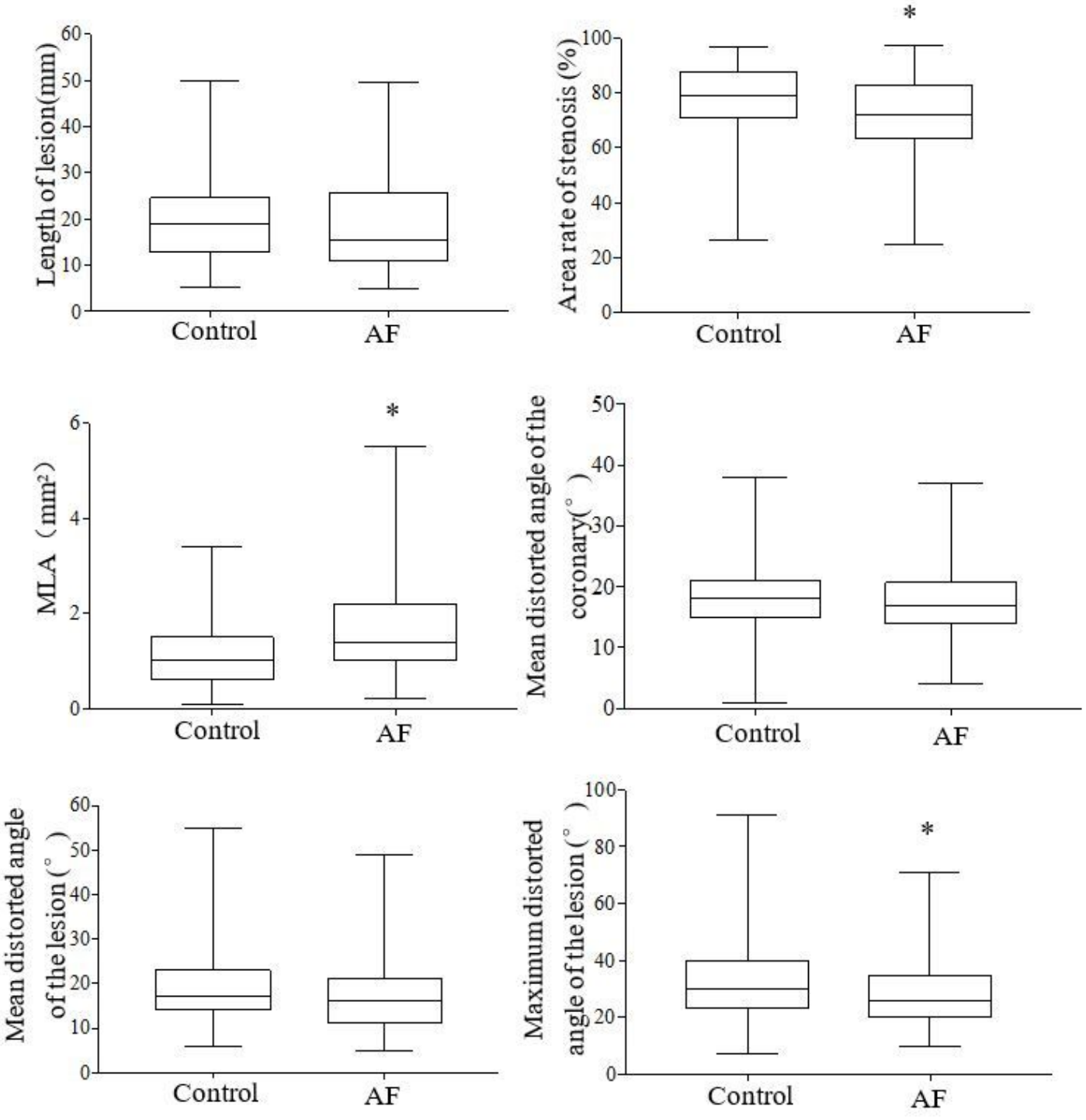

Figure 6

The anatomy of the coronary and lesion in two groups of patients including length of the lesion, area rate of stenosis, MLA, mean distorted angle in coronary and lesion and maximum distorted angle in the lesion.