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ORIGINAL RESEARCH

Evaluation of the Relationship Between Aortic Stiffness and Elasticity and Left Ventricular Functional Parameters in Patients with ANOCA Using CCTA

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Objective: To analyze the clinical value of coronary CT angiography (CCTA) for evaluating aortic stiffness and elasticity in patients with angina and non-obstructive coronary artery (ANOCA).

Methods: The case data of 120 patients who were diagnosed with ANOCA and underwent CCTA in our hospital were collected and set as the case group, and 86 healthy subjects who underwent medical check-up and ANOCA testing in our hospital during the same period were set as the control group. The differences in CCTA indices of ascending aortic stiffness and aortic elasticity, left ventricular function indices of left ventricular ejection fraction (LVEF) and cardiac output (CO) were compared between the two groups.

Results: The arterial compliance (AC) and arterial distensibility (AD) values in the case group were significantly lower than those in the control group, while arterial stiffness (β) value was significantly higher in the case group compared to the control group ($P<0.05$). The LVEF and CO values of patients in the case group were significantly lower than those in the control group ($P<0.05$). The CCTA indices AC and AD of patients in the case group exhibited a significant positive correlation with their LVEF ($r=0.133$, $r=0.062$, $P<0.05$), while β showed a negative correlation with LVEF ($r=-0.092$, $P=0.005$).

Conclusion: Aortic stiffness and elasticity in CCTA indices of ANOCA patients exhibited significant alterations, and the correlation analysis suggested a correlation of CCTA aortic stiffness and elasticity indices with left ventricular performance indices.

Keywords: coronary CT angiography, angina and non-obstructive coronary artery, aortic stiffness, aortic elasticity, diagnostic efficacy

Introduction

The coronary microcirculatory system comprises the anterior arterioles, arterioles, venules, and capillaries. Myocardial ischemia represents a category of diseases characterized by reduced cardiac blood perfusion as a typical clinical symptom, and patients experiencing myocardial ischemia may manifest signs such as hypoxia and abnormalities in energy metabolism, constituting a pathological state of the heart.[1,2] In recent years, due to adjustments in residents' lifestyles and dietary patterns, there has been a rising trend in the global incidence of myocardial ischemia, making it a common and prevalent ailment among middle-aged and elderly individuals, with some young people aged 20–30 years exhibiting manifestations of myocardial ischemia.[3,4]

Clinical practice indicates that some patients with myocardial ischemia may be suspected of coronary heart disease due to the onset of angina symptoms, and it is recommended to confirm this suspicion through coronary angiography; however, data also

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indicate that 40% of patients with angina undergoing coronary angiography do not exhibit coronary artery vascular obstruction, which inadvertently leads to the wastage of medical resources and imposes unnecessary economic burden and suffering on patients.[5,6] Coronary computed tomography angiography (CCTA) has emerged in recent years as a non-invasive means of detecting coronary artery disease. Clinical studies have validated its high diagnostic sensitivity for most coronary artery diseases, particularly its efficacy in excluding certain coronary artery lesions.[7,8] In the past few decades, extensive prospective clinical studies have substantiated the significant utility of CCTA in the diagnosis of coronary heart disease, risk assessment, and treatment guidance, and the Society of Cardiovascular Computed Tomography updated their expert consensus in 2021.[9,10] Presently, there is a paucity of research regarding the application of CCTA in angina and non-obstructive coronary artery (ANOCA). Further elucidation is required to ascertain whether this diagnostic modality can provide diagnostic value for ANOCA by quantifying indicators such as aortic stiffness and elasticity in suspected ANOCA patients. This study retrospectively analyzed the clinical value of CCTA in assessing aortic stiffness and elasticity in ANOCA patients, evaluated the correlation between CCTA-related parameters and left ventricular function indices, and explored the application efficacy of CCTA aortic stiffness and elasticity indices in the differential diagnosis of ANOCA.

Materials and Methods

Study Design

The present study is a retrospective analysis, with the observation period spanning from July 2020 to July 2023. Patients diagnosed with ANOCA who underwent both CCTA and left ventricular function testing during this period in our hospital were selected as the case group. The current study was approved by Affiliated Hangzhou First People's Hospital, Westlake University School of Medicine Ethics Committee (Approval No. KY-20240408-0124-01). All patients provided written informed consent prior to enrollment in the study. All procedures were conducted in accordance with the Declaration of Helsinki. Healthy individuals who underwent CCTA testing during the same period in our hospital were selected as the control group. Specific inclusion and exclusion criteria are as follows:

Inclusion criteria for the case group: (1) Patients who were diagnosed with ANOCA in our hospital; (2) Patients who underwent CCTA for assessment of aortic stiffness and elasticity; (3) Patients who underwent evaluation of left ventricular function; (4) Patients with complete data, including sex, age, medical history, smoking history, medication history, etc. Exclusion criteria for the case group: (1) Patients with previous coronary artery bypass grafting or percutaneous coronary intervention; (2) Patients with poor quality CT scan images hindering research; (3) Patients with incomplete clinical data.

Inclusion criteria for the control group: (1) Participants who underwent CCTA for assessment of aortic stiffness and elasticity; (2) Participants who underwent evaluation of left ventricular function; (3) Participants with complete demographic data, including sex, age, medical history, smoking history, medication history, etc. Exclusion criteria for the control group were the same as those for the case group.

Eligible Participants

According to the aforementioned inclusion and exclusion criteria, after the screening of the medical records utilizing the hospital's information system, 120 patients were included in the case group, and 86 participants were included in the control group. The general clinical data of patients in the case and control groups, such as sex, age, and body mass index (BMI), were compared between groups, showing no statistically significant differences ($P>0.05$), indicating comparability between the two groups, as shown in Table 1.

Data Collection

The baseline clinical data (sex, age, BMI, medication history, disease history, blood biochemical indices) of patients in the case and control groups were collected by means of the hospital information system.

Indicators reflecting aortic stiffness and aortic elasticity in CCTA were collected from both groups of patients. All patients underwent CCTA testing using a Canon Aquilion ONE CT scanner with the following parameters: tube voltage of 120 kV, automatic tube current modulation, rotation time of 0.35 s, collimation width of 0.5 mm × 320, pitch of 0.656,

Table 1 Comparison of the Baseline Clinical Data of Patients in the Case and Control Groups

General Clinical Data		Case Group (n=120)	Control Group (n=86)	*SMD*	P
Sex	Male	69 (57.50%)	46 (53.49%)	0.064	0.562
	Female	51 (42.50%)	40 (46.51%)		
Mean age (years)		61.29±5.11	61.34±5.18	0.010	0.893
Mean body mass index (kg/m^2)		23.01±2.39	22.98±2.21	0.013	0.792
Medical history	Hypertension	78 (65.00%)	46 (53.49%)	0.235	0.096
	Diabetes	36 (30.00%)	21 (24.42%)	0.125	0.377
	Cerebrovascular disease	11 (9.17%)	8 (9.30%)	0.004	0.974
	Family history of cardiovascular disease	51 (42.50%)	40 (46.51%)	0.081	0.567
Medication history	Aspirin	51 (42.50%)	32 (37.21%)	0.108	0.812
	Statins	31 (25.83%)	21 (24.42%)	0.033	0.631
Blood biochemical index (mmol/L)	Total cholesterol	4.51±1.23	4.26±1.51	0.181	0.211
	Fasting blood-glucose	6.23±1.56	6.01±1.55	0.142	0.541
	Blood uric acid	334.56±56.23	326.59±81.23	0.114	0.102

and reconstruction slice thickness of 0.5 mm. Patients were positioned supine, monitored via electrocardiography (ECG), and administered 60–80 mL of iohexol (350 mgI/mL) via the elbow vein at a flow rate of 4–5 mL/s, followed by 30 mL of saline. Prospective ECG-gated scanning was performed, covering the region from the aortic root to 1–2 cm below the cardiac apex. Image reconstruction was performed using a standard convolution kernel and analyzed on a dedicated post-processing workstation. Aortic stiffness and elasticity were evaluated at the ascending aorta, specifically at a transverse section 20 mm above the aortic valve. Aortic cross-sectional areas were measured during systole and diastole, while peripheral systolic and diastolic blood pressures were simultaneously recorded. The selected parameters included AC, AD, and β. AC was calculated as (maximum artery area during cardiac systole - minimum artery area during cardiac diastole)/(peripheral systolic pressure - peripheral diastolic pressure),[11] AD was calculated as [(maximum artery area during cardiac systole - minimum artery area during cardiac diastole)/minimum artery area during cardiac diastole]/(peripheral systolic pressure - peripheral diastolic pressure),[12] and β was calculated as In (peripheral systolic pressure/peripheral diastolic pressure × 0.77)/[(maximum artery area during cardiac systole - minimum artery area during cardiac diastole)/minimum artery area during cardiac diastole] × 10^{-3}).[13]

The left ventricular function indices of left ventricular ejection fraction (LVEF) and cardiac output (CO) were collected in both groups. Left ventricular function was assessed using the same CCTA system (Canon Aquilion ONE), acquiring volumetric data throughout the entire cardiac cycle under electrocardiographic gating. Post-processing was performed with dedicated cardiac function analysis software (eg, Vitrea or Syngo.via), utilizing semi-automated contour-tracking technology to delineate the endocardial border of the left ventricle. Left ventricular volumes were measured at both end-diastole and end-systole. LVEF was calculated using the formula: LVEF (%) = [(end-diastolic volume − end-systolic volume) / end-diastolic volume] × 100%. CO was calculated as CO (L/min) = stroke volume (SV) × heart rate (HR), where SV was determined by subtracting end-systolic volume from end-diastolic volume. All measurements were independently conducted by two radiologists with over five years of CCTA experience. In cases of discrepancy, a third senior radiologist rendered the final decision.

Quality Control

To prevent errors in data collection and entry by a single person, this study employed two persons for data collection and entry. Both individuals involved were cardiovascular medical personnel who meticulously cross-checked the data to ensure accurate input.

Expected Outcomes and Statistical Analysis

The expected outcomes of this study involve significant differences in CCTA-related indices AC, AD, and β-values between the case and control groups. Additionally, both groups exhibit significant differences in LVEF and CO values. Furthermore, there is a certain correlation of CCTA indices with LVEF and CO values in case group patients. CCTA indices demonstrate a certain degree of efficacy in the diagnosis of ANOCA.

In this study, statistical analyses were conducted using SPSS 21.0. The Shapiro–Wilk test and Q-Q plot method were employed to assess the normality of continuous variables, including age, BMI, and biochemical parameters. Verification confirmed that variables such as age and BMI followed a normal distribution and were expressed as mean ± standard deviation (SD). Inter-group comparisons were performed using the *t*-test to evaluate patient balance, while standardized mean difference (SMD) analysis was conducted for baseline characteristics ($0.1 \le SMD < 0.2$ indicating a small difference, $0.2 \le SMD < 0.5$ a moderate difference, and $SMD \ge 0.5$ a large difference). Categorical variables were presented as rates and analyzed using the chi-square test. Correlation analyses were conducted using Spearman correlation. A statistical significance was set at $P<0.05$. The diagnostic performance of CCAT indices in predicting ANOCA was assessed using Receiver Operating Characteristic (ROC) curve analysis, with the optimal cutoff value determined by the Youden Index method, defined as the point maximizing the sum of sensitivity and specificity minus one.

Results

Differences in CCTA Indices of the Case and Control Groups

The AC and AD values in the case group were significantly lower than those in the control group, while β was significantly higher in the case group compared to the control group ($P<0.05$) (Figure 1).

Differences in Left Ventricular Function Indices of the Case and Control Groups

After collecting the data from the case information system for comparison, the results showed that the LVEF and CO values of patients in the case group were significantly lower than those in the control group, exhibiting statistically significant difference ($P<0.05$) (Figure 2).

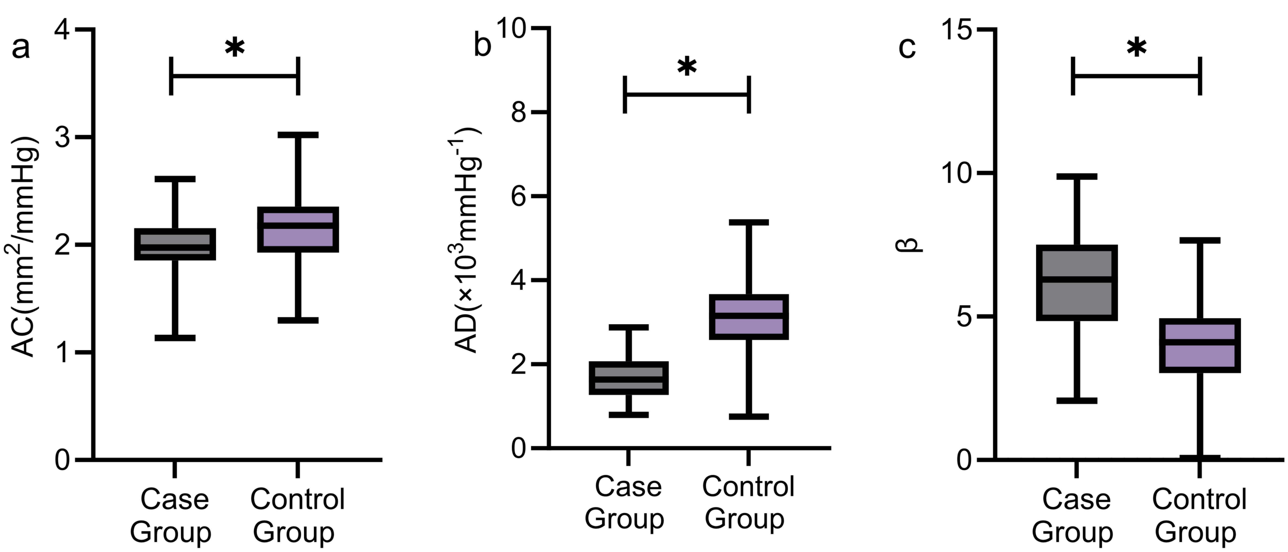

Figure 1 Differences in CCTA indices of the case and control groups. The AC (**a**) and AD (**b**) values in the case group were significantly lower than those in the control group, while β (**c**) was significantly higher in the case group compared to the control group ($P<0.05$). * denotes statistically significant differences between groups.

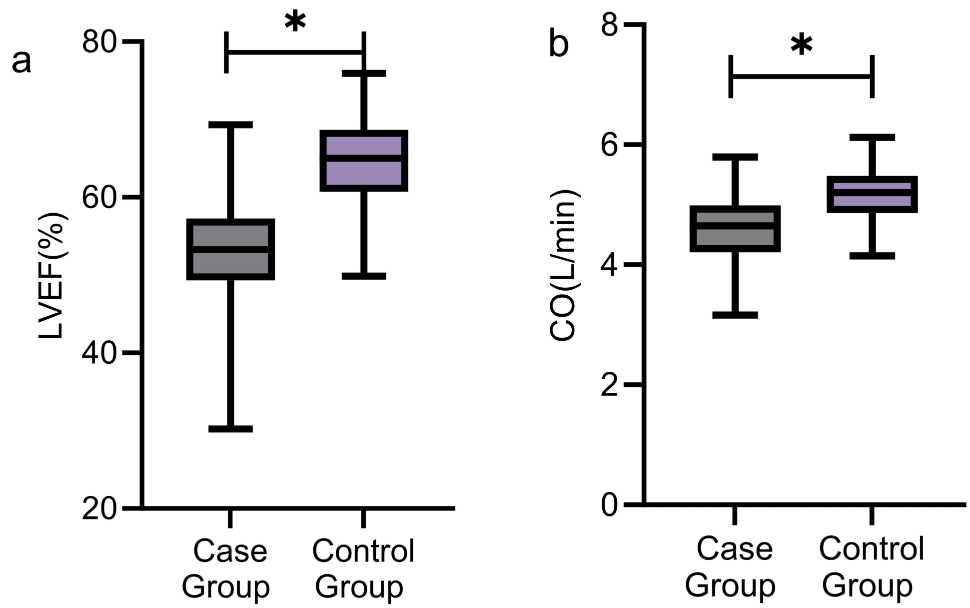

Figure 2 Differences in left ventricular function indices of the case and control groups. The LVEF (**a**) and CO (**b**) values of patients in the case group were significantly lower than those in the control group (P<0.05). * denotes statistically significant differences between groups.

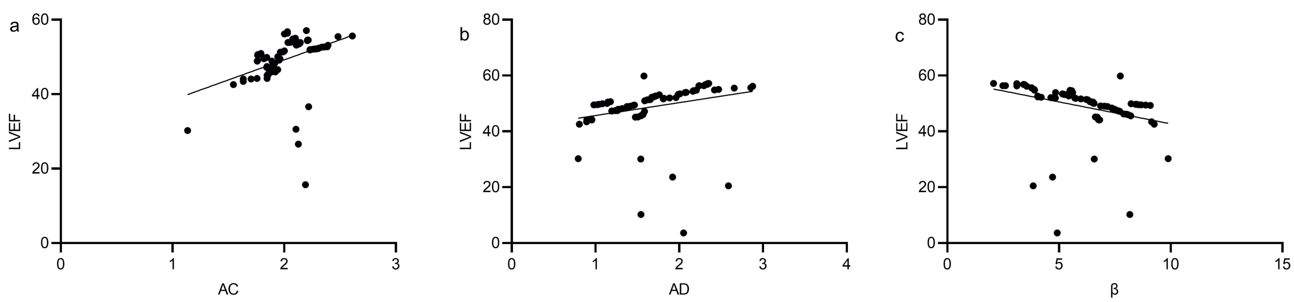

Figure 3 Correlation analysis of CCTA indices and LVEF in the case group. In the case group, AC (**a**) and AD (**b**) were positively correlated with LVEF, while β (**c**) was negatively correlated with LVEF (P<0.05).

Correlation Analysis of CCTA Indices and Left Ventricular Function Indices in the Case Group

The CCTA indices AC and AD of patients in the case group exhibited a significant positive correlation with their LVEF (r=0.133, r=0.062, P<0.05), while β showed a negative correlation with LVEF (r=−0.092, P=0.005) (Figure 3). AC and AD of patients in the case group demonstrated a positive correlation with CO (r=0.506, r=0.502, P<0.05), whereas β exhibited a negative correlation with LVEF (r=−0.491, P<0.05) (Figure 4).

Analysis of Clinical Efficacy of CCTA Indices in Predicting ANOCA

The ROC curve was plotted to calculate the clinical efficacy of CCTA indices in predicting ANOCA, and the results showed that the AUC for AC diagnosis was 0.648 (95% CI=0.573–0.723) (P<0.05), for AD diagnosis was 0.927 (95% CI=0.890–0.965) (P<0.05), and for β diagnosis was 0.817 (95% CI=0.756–0.878) (P<0.05) (Table 2, Figure 5).

Discussion

Angina pectoris is the most prevalent symptom of ischemic heart disease, afflicting approximately 112 million people worldwide.[14] A study conducted abroad suggests that approximately 70% of angina patients suffer from ANOCA.[15] A study conducted in China also indicates that the prevalence of ANOCA domestically is approximately 20%.[16] Patients

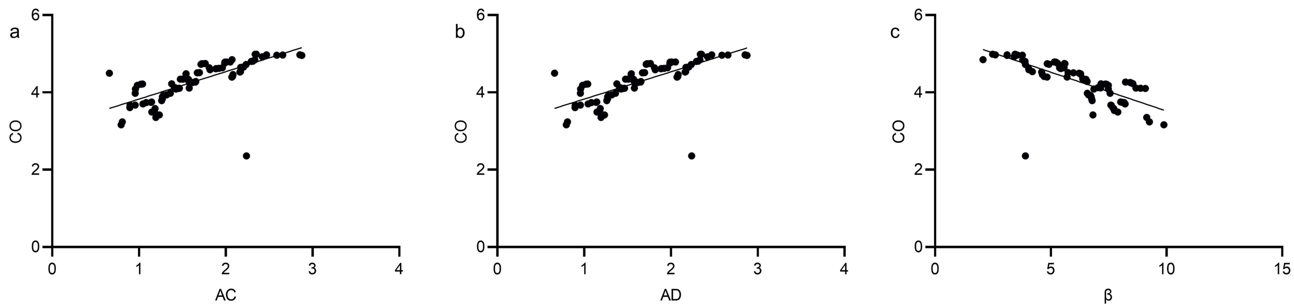

Figure 4 Correlation analysis of CCTA indices and CO in the case group. In the case group, AC (**a**) and AD (**b**) were positively correlated with CO, while β (**c**) was negatively correlated with CO (P<0.05).

with ANOCA often exhibit a reduced emphasis on their condition due to the absence of obstructive coronary stenosis, leading to a lack of specific health management and pharmacological interventions. However, several studies[17,18] have confirmed that the incidence of cardiovascular events and all-cause mortality rate in ANOCA patients are significantly higher than in the general population, which has gradually garnered attention from healthcare professionals in recent years.

Coronary angiography is considered the gold standard for assessing coronary artery occlusion status, but this invasive method exhibits poor repeatability and is not conducive to widespread adoption. In recent years, with the continuous development of non-invasive techniques for evaluating functional status of coronary artery, CCTA, characterized by its non-invasiveness, excellent repeatability, and high sensitivity, has been widely employed in assessing coronary artery conditions.[19,20] Existing research[21] has indicated that CCTA effectively reflects the nature of coronary artery plaques, distinguishes plaque regions into fibrous tissue, adipose tissue, and calcified tissue through spectral information, and more intuitively displays the distribution images of various tissue components within the plaque, which provides quantitative information for the assessment of the severity of coronary heart disease. Additionally, another research[22] suggests that CCTA can be utilized for the measurement of atrial and ventricular volumes, demonstrating significant utility in the diagnosis of ascending aortic diseases. In this study, the application value of CCTA in ANOCA patients was evaluated, and the results indicated that patients in the case group had significantly lower AC and AD values and higher β value compared with the healthy control group, suggesting marked differences in aortic stiffness and elasticity between patients in the case group and healthy individuals. The authors of this research analyzed that ascending aortic lesions have similar pathological changes to atherosclerosis, such as vascular smooth muscle disappearance, extracellular matrix mucoid transformation, and elastic fiber degradation, and these aforementioned lesions may occur independently or manifest in a mixed pattern. Prolonged pathological states subject the vessels to stress, leading to the transformation of elastic vessels into stiffer collagen components, thereby reducing vascular elasticity and inducing plastic changes.[23,24] The decrease in elasticity and increase in stiffness are both specific manifestations of arterial dysfunction. Optimal vascular elasticity is a prerequisite for the reversible expansion and relaxation of arteries during the cardiac cycle, which has positive implications for reducing cardiac workload and inhibiting distal arterial pulsations. In this study, the AC and AD values of patients in the case group were significantly lower than those in the control group, while the β value was higher than in the control group. This suggested that patients in the case group exhibited significantly lower aortic elasticity and noticeably higher stiffness compared to the control group. These findings are consistent with the results of other scholars' research.[25]

Table 2 Analysis of Clinical Efficacy of CCTA Indices in Predicting ANOCA

Diagnostic Indices	AUC	SE	95% CI	P	Cut-Off Values
AC	0.648	0.038	0.573–0.723	<0.001	2.048
AD	0.927	0.019	0.890–0.965	<0.001	2.250
β	0.817	0.031	0.757–0.877	<0.001	4.887

Abbreviations: CCTA, coronary computed tomography angiography; ANOCA, angina and non-obstructive coronary artery; AUC, area under the curve; SE, standard error; 95% CI, 95% confidence interval; AC, arterial compliance; AD, arterial distensibility; β, arterial stiffness.

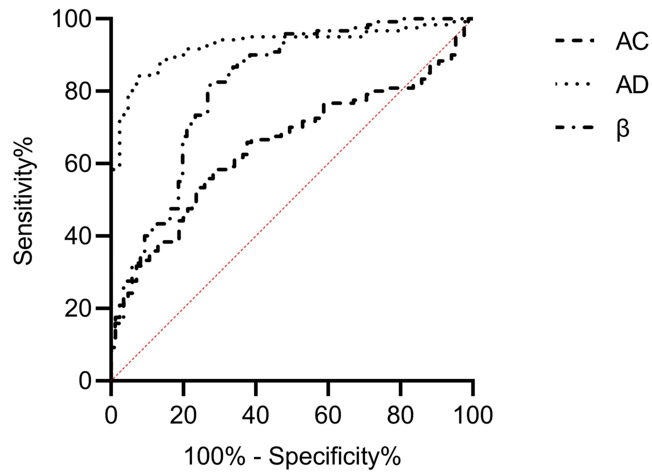

Figure 5 Clinical efficacy of CCTA indices in predicting ANOCA. The AUC for AC diagnosis was 0.648 (95% CI=0.573–0.723), for AD diagnosis was 0.927 (95% CI=0.890–0.965), and for β diagnosis was 0.817 (95% CI=0.756–0.878).

In this study, the further results indicated significant differences in left ventricular function indices between the case and control groups, with both LVEF and CO values notably higher in the control group. A controlled study conducted on ANOCA patients[26] found that the majority of patients with ANOCA experienced symptoms of chest pain and chest tightness, and the Gensini score had a positive significance in evaluating the coronary artery condition of patients with ANOCA; moreover, the LVEF and Gensini score of such patients differed considerably from those of the general population, which is similar to the results of the present study. The authors of this study analyzed that the cardiomyocytes of patients with ANOCA are in a prolonged stage of ischemia and hypoxia, significantly affecting both systolic and diastolic cardiac functions, resulting in a decrease in cardiac systolic and diastolic functions. Furthermore, in the state of myocardial ischemia, the cardiomyocytes may undergo swelling and fibrotic lesions, thereby resulting in myocardial stiffening, which affects the early active relaxation of the myocardium, subsequently leading to secondary augmentation of atrial contraction and a decrease in left ventricular contractility. The correlation analysis in the study indicated that the CCTA indices of ANOCA patients were closely associated with their left ventricular functional indices, thereby indirectly confirming that changes in aortic elasticity and stiffness may impact the left ventricular function of ANOCA patients. Furthermore, the correlation coefficients of CCTA parameters AC and AD with LVEF in the case group ($r=0.133$, $r=0.062$) reached statistical significance ($P<0.05$); however, their relatively low values suggest that this correlation should be interpreted with caution in clinical applications. This may be attributed to the large sample size, where even small effect sizes can achieve statistical significance. In contrast, the correlation coefficients of AC and AD with CO ($r=0.506$, $r=0.502$) were comparatively higher, indicating a potentially stronger physiological relationship between aortic elasticity parameters and CO. Future studies should further investigate the clinical implications of these associations while considering potential confounding factors.

To investigate the clinical efficacy of CCTA in diagnosing ANOCA, the ROC curves for AC, AD, and β values were depicted in this study, indicating good diagnostic efficacy for these indices. The authors of this study analyzed and believed that arterial elasticity and stiffness, as the crucial parameters for assessing arterial wall function, were closely associated with conditions such as hypertension, atherosclerosis, and coronary heart disease. Furthermore, research indicated that decreased aortic elasticity was an independent risk factor for inducing coronary heart disease. The evaluation of individual arterial elasticity and stiffness through CCTA is of positive significance for distinguishing ANOCA.

It is noteworthy that this study only analyzed the correlation of aortic stiffness and elasticity indices with left ventricular function parameters in the case group, aiming to elucidate their intrinsic associations within ANOCA patients for a deeper understanding of disease mechanisms. Future studies may incorporate control group data for a comprehensive correlation analysis to further validate the variation patterns of these parameters across different populations and their clinical significance, thereby providing a more robust foundation for the diagnosis and differentiation of ANOCA.

Aortic stiffness and elasticity in CCTA indices of ANOCA patients exhibited significant alterations, and the correlation analysis suggested a correlation of CCTA aortic stiffness and elasticity indices with left ventricular performance indices. CCTA aortic stiffness and elasticity indices may be considered to be applied in the differential diagnosis of ANOCA.

In this study, CCTA was utilized to measure aortic stiffness and elasticity parameters, offering a novel approach to ANOCA diagnosis. Compared with conventional diagnostic methods such as coronary angiography, exercise stress test, and coronary flow reserve measurement, CCTA demonstrates distinct advantages in assessing aortic stiffness and elasticity, including its noninvasive nature, high repeatability, and operational simplicity. Although conventional coronary angiography remains the gold standard for coronary assessment, it is an invasive procedure incapable of directly evaluating microvascular dysfunction. Exercise stress test is constrained by limited sensitivity and specificity, while coronary flow reserve measurement requires specialized equipment and advanced operational techniques. In addition to assessing the severity of coronary artery stenosis, CCTA enables supplementary functional evaluation for ANOCA patients through parameters such as AC, AD, and β values, as validated in this study. Notably, the AD value demonstrated high diagnostic efficacy (AUC=0.927), suggesting its potential as a practical screening tool to reduce unnecessary invasive procedures. Moreover, CCTA enables the simultaneous acquisition of anatomical and functional parameters, providing a more comprehensive basis for clinical decision-making. However, its limitations, including radiation exposure and renal function requirements, necessitate further research to optimize scanning protocols, striking a balance between diagnostic efficacy and safety. This is a retrospective, single-centered study and lacks follow-up information. It is proposed that in subsequent stages, a prospective, multicenter, long-term follow-up study will be conducted to provide further evidence for the application of CCTA in the differential diagnosis of ANOCA.

Data Sharing Statement

All data generated or used during the study appear in the submitted article.

Ethics Approval and Informed Consent

The current study was approved by Affiliated Hangzhou First People's Hospital, Westlake University School of Medicine Ethics Committee (Approval No. KY-20240408-0124-01). All patients provided written informed consent prior to enrollment in the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Aizhu Sheng and Lili Zhang are co-first authors for this study. The authors declare that they have no competing interests.

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