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RESEARCH ARTICLE

Diagnosis of Coronary Artery Disease by Acoustic Analysis of Turbulent Murmur Caused by Coronary Artery Stenosis: A Single Center Study from China

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Abstract

Aim: Intracoronary murmur results from turbulent flow due to coronary artery narrowing. This study evaluated the diagnostic performance of a method for acoustic analysis of turbulent murmur caused by coronary artery stenosis in coronary artery disease (CAD) in Chinese populations.
Method: Patients admitted to the cardiovascular department of the Sixth Medical Center of the Chinese People's Liberation Army General Hospital between September 2021 and June 2022 for elective coronary angiography were prospectively enrolled. A digital electronic stethoscope was used to record heart sounds before angiography. Quantitative coronary angiography (QCA) served as the "gold standard" for CAD diagnosis to evaluate the diagnostic performance of the acoustic analysis method for CAD.
Results: A total of 452 patients had complete QCA and heart sound data. The final interpretation results of the acoustic analysis method indicated 310 disease cases and 142 normal results. Increasing the cut-off values of coronary artery diameter stenosis from 30% to 50%, 70%, and 90% increased the sensitivity and NPV of the acoustic analysis method; the sensitivity was 75.6%, 81.9%, 83.3%, and 85.7%, respectively; the NPV was 33.1%, 57.0%, 69.7%, and 88.0%, respectively; the specificity and PPV decreased (specificity of 75.8%, 70.4%, 51.0%, and 37.5%, respectively; PPV of 95.2%, 89.0%, 69.4%, and 32.9%, respectively); and the AUC values were 0.757, 0.762, 0.672, and 0.616, respectively. The sensitivity of the acoustic analysis method for one-vessel disease was 86.6% when the cut-off value was 50%. The sensitivity for identifying left anterior descending coronary artery lesions was best, at 90.7%. The sensitivity for identifying isolated coronary artery branch lesions was 66.7%, whereas the sensitivity for identifying three-vessel disease in multi-vessel coronary artery lesions was better, at 82.9%.
Conclusion: Acoustic analysis of turbulent murmur caused by coronary artery stenosis for diagnosis of CAD may have favorable performance in the Chinese population. This method has good performance in CAD diagnosis with a cut-off coronary artery diameter for stenosis of 50%.

Keywords: Coronary artery disease; coronary artery stenosis; heart sounds; non-invasive testing

Introduction

Cardiovascular disease poses a substantial economic burden, and threatens human health and life [1]. A recent report has indicated that approximately 330 million people have cardiovascular diseases in China, including 11.39 million people with coronary artery disease (CAD) [2]. CAD is caused by coronary artery atherosclerosis, which leads to myocardial ischemia, hypoxia, or necrosis. In recent years, some studies have reported acoustic analysis of turbulent murmur caused by coronary artery stenosis – a promising new method for CAD diagnosis [3–5].

Research on the use of acoustic methods for CAD diagnosis dates back to the 1960s. At that time, Dock et al. [6] detected a diastolic murmur associated with coronary stenosis by using phonocardiography. Later, other authors reported heart murmurs similar to Dock's murmur [7, 8]. However, their research findings were not well explained or verified, probably because of the limited detection technology and analytic methods available at that time. In recent years, with the updating and development of acoustic detection equipment and analysis methods, the diastolic murmur signal associated with coronary artery stenosis has been detected with modern acoustic detection equipment and analysis methods [3, 4, 9, 10].

The diagnosis of CAD through acoustic analysis of turbulent murmurs caused by coronary artery stenosis is easy to understand. The coronary blood supply is delivered mainly during heart diastole [11]. Intracoronary blood flow normally shows a laminar flow pattern. However, when specific stenosis occurs in the coronary artery branch, the laminar flow becomes turbulent and can produce turbulent murmur in the coronary arteries [11, 12]. Previous studies have indicated that intravascular murmur associated with 25–95% stenosis can be detected with acoustic detection equipment [12, 13]. A lesion with <25% stenosis does not substantially influence the blood flow pattern. A lesion with >95% stenosis is due to less quantitative blood flow through the stenosis. Both conditions are unlikely to produce a detectable turbulent murmur associated with vascular stenosis [12, 13].

The acoustic analysis method for CAD diagnosis has the advantages of safety, portability, low cost, and an absence of radiation [11, 14]. Currently, limited clinical research on acoustic methods in CAD diagnosis has been performed. Moreover, the study populations had a low prevalence of coronary heart disease, and comprised mainly Europeans and Americans [10, 15, 16]. No clinical research report has focused on a Chinese population. Therefore, this study used quantitative coronary angiography (QCA) as a diagnostic standard to evaluate the performance of the acoustic analysis method of turbulent murmurs caused by coronary artery stenosis in Chinese inpatients.

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Materials and Methods

Study Population

A total of 468 patients who planned to undergo elective invasive coronary angiography (ICA) at the cardiovascular department of the Sixth Medical Center of the Chinese People's Liberation Army General Hospital between September 2021 and June 2022 were enrolled prospectively. The exclusion criteria were as follows:

1. Patients with congenital heart disease or valvular heart disease
2. Patients with arrhythmias such as atrial fibrillation, atrial flutter, or ventricular tachycardia
3. Patients with severe lung disease or thoracic deformity
4. Patients with a history of coronary stenting, coronary artery bypass grafting, or pacemaker implantation
5. Patients who refused to participate in the trial

We collected baseline data, heart sounds, and coronary angiography data for each enrolled patient.

The study involving human participants was reviewed and approved by the Ethics Committee of the Sixth Medical Center of the People's Liberation Army General Hospital (No. HZKY-PJ-2021-21). We obtained consent from all patients before study participation.

Study Methods

The patients who met the trial criteria received standard ICA after heart sound data acquisition and storage. Using QCA as the diagnostic standard, we divided the patients on the basis of five grades and calculated the sensitivity, specificity, PPV, NPV, accuracy, and AUC values of the acoustic analysis method at several cut-off values (Figure 1).

Collection of Heart Sound Data

Heart sound data were collected from each participant before ICA with an advanced digital electronic stethoscope (3M™ Littmann Model 3200) in a quiet environment. The participants were in supine position. We collected the heart sounds from nine sites in the third, fourth, and fifth intercostal spaces of the right sternum border, the left sternum border, and the left midclavicular line. Each site was recorded for 40 seconds. The collected heart sound data were sent to a portable computer via Bluetooth and stored in the supporting heart sound signal processing and analysis software.

Invasive Coronary Angiography

Multiple angiographic views of the left and right coronary arteries were recorded in 1024×1024 pixel format at 15 to 30 frames per second, and stored for later analysis. Experienced interventional physicians blinded to the heart sound data analyzed the QCA data collected via ICA. The degree of coronary artery stenosis was divided into five grades according to the QCA data as follows. Grade 0 indicated <30% stenosis of the largest diameter of all coronary primary

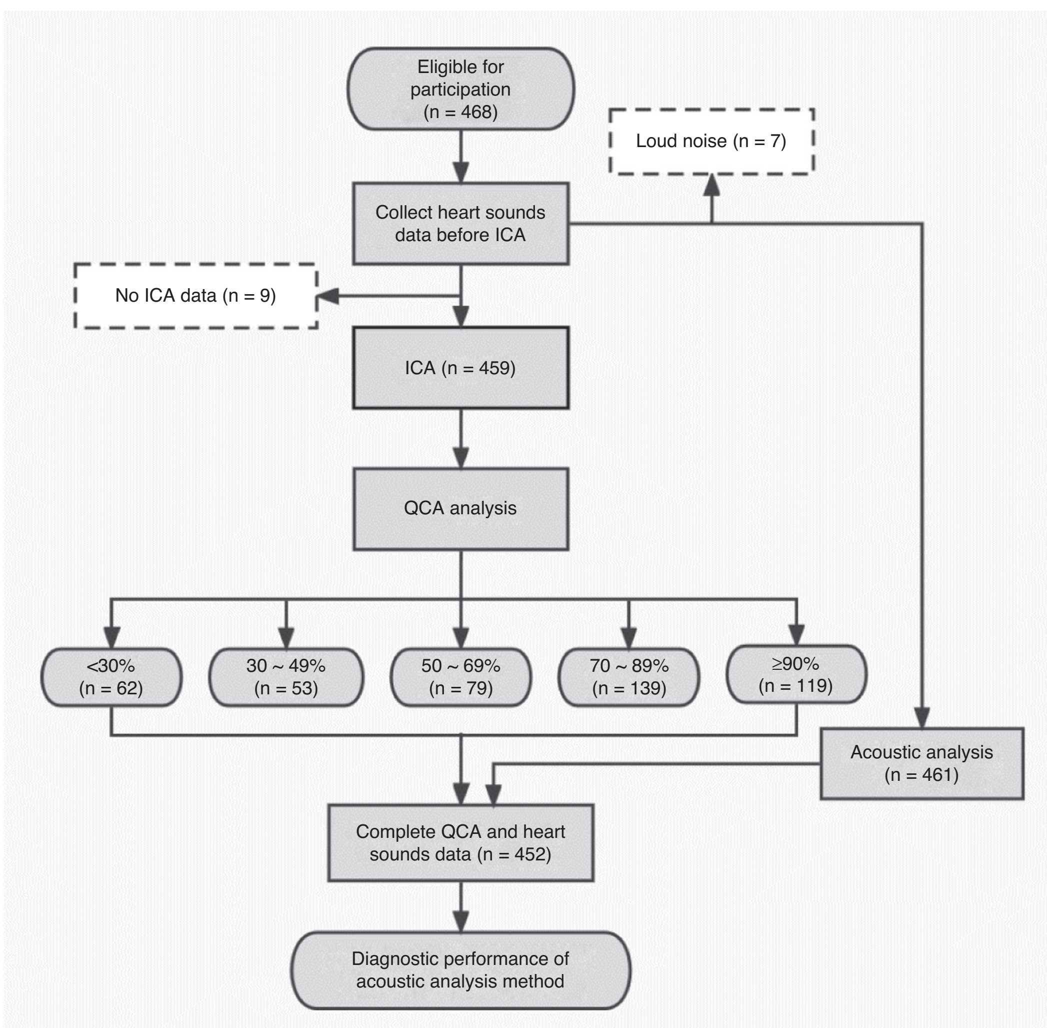

Figure 1 Flow Chart of this Study.
ICA: invasive coronary angiography; QCA: quantitative coronary angiography.

and branch lesions. Grades 1–4 indicated one or multiple coronary primary and/or branch lesions, with grade 1: maximum diameter stenosis range of 30–49%; grade 2: maximum diameter stenosis range of 50–69%; grade 3: maximum diameter stenosis range of 70–89%; and grade 4: maximum diameter stenosis range of 90–100%. The patients with grade 0 stenosis were considered not to have CAD. Patients with grade 1 stenosis were considered to have non-obstructive CAD. Patients with grade 2–4 stenosis were considered to have obstructive CAD, and those with grade 3 or 4 stenosis were considered to have severe obstructive CAD. (Of note, coronary vessels with an original diameter <2.5 mm were excluded.)

Interpretation of Acoustic Analysis Results

Trained staff blinded to the patients' clinical and QCA data used a digital electronic stethoscope and supporting Zargis Cardioscan™ software to interpret the heart sound data. The software uses an acoustic algorithm to automatically identify the systolic and diastolic phases of the heart. On the basis of the heart sound spectrum characteristics of 25 patients with obstructive CAD and 20 participants without CAD in the preliminary experiment, combined with previous research results [17–19], we determined the characteristics of diastolic turbulent murmur associated with coronary artery stenosis. The time-domain characteristics of the diastolic turbulent murmur were generally 200–300 ms after the second heart sound, and the frequency-domain characteristics were usually 300–800 Hz. We used the presence or absence of the above characteristics of murmur signals to distinguish normal and diseased states. Normal indicates that the murmur signals described above were not observed in the heart sound data collected from the nine auscultation sites during diastole. Diseased indicates that the murmur signals appeared regularly during diastole in the heart sound data collected from at least one of the nine auscultation sites. Two staff members independently reviewed the acoustic analysis results of all participants, and discordant diagnoses were resolved by an independent third staff member. Examples of normal and diseased diagnoses are shown in Figure 2.

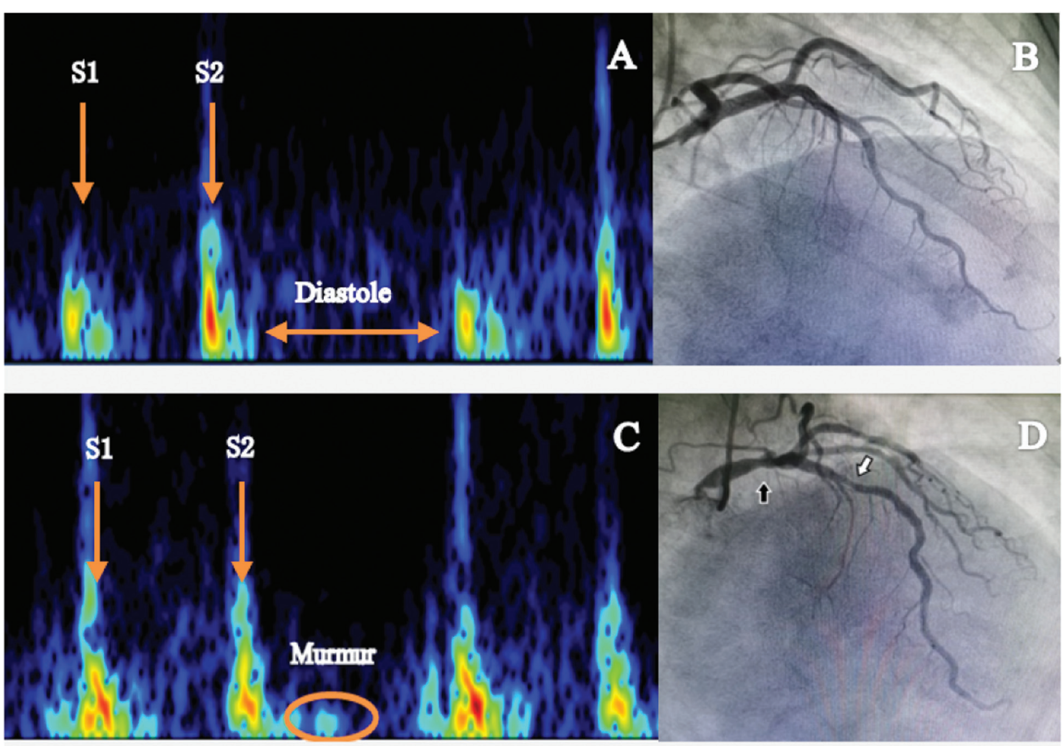

Figure 2 Acoustic Analysis Results and Corresponding Angiograms.
Patient 1 (A–B): acoustic analysis (A) indicating no discernible diastolic murmur signal detected after S2; angiogram (B) indicating normal coronary artery anatomy. Patient 2 (C–D): acoustic analysis (C) indicating a discernible diastolic murmur signal after S2; angiogram (D) demonstrating two distinct significant stenoses in the proximal and middle part of the left anterior descending coronary artery. S1: first heart sound; S2: second heart sound.

Statistical Analysis

The data were analyzed in SPSS version 26.0 (SPSS Inc., Chicago, IL, USA) and MedCalc® Statistical Software version 20.019 (MedCalc Software Ltd, Ostend, Belgium). Continuous variables are presented as mean ± standard deviation or as median (and 25th and 75th percentiles) for data not normally distributed. Categorical variables are presented as frequency and percentage. We calculated the sensitivity, specificity, PPV, NPV, accuracy, and AUC value of the acoustic analysis method with different stenosis cut-off values by using QCA as the diagnostic criterion. The statistical differences across the five groups (stenosis <30%, stenosis 30–49%, stenosis 50–69%, stenosis 70–89%, and stenosis ≥90%) were evaluated with analysis of variance. The AUC value was used as a metric to determine the overall diagnostic performance of the acoustic analysis method. The odds ratio (OR) was calculated to compare characteristic acoustic signals with other predictors with logistic regression analysis. Two-sided P values < 0.05 were considered to indicate statistical significance.

Results

Patient Characteristics

A total of 468 patients were enrolled in the study. We excluded six (3.4%) patients. (Nine patients did not undergo ICA, and we were unable to interpret the acoustic analysis results because of noise in seven patients.) A total of 452 patients ultimately had complete QCA and heart sound data. The final interpretation results of the acoustic analysis method indicated 310 cases of disease and 142 normal findings. The baseline characteristics of the patients are detailed in Table 1. The study population was mainly male (68.1%), 61.1 ± 10.0 years of age, and mildly overweight (BMI: 25.6 ± 3.8 kg/m^2). Common serum laboratory indexes, such as hemoglobin (137.9 ± 17.9 g/L) and platelets (220.2 ± 60.5 × 109/L), were generally within normal ranges. The left ventricular function ranged from abnormal to normal (ejection fraction 53.5 ± 19.6). The traditional CAD risk factors were diverse and included hypertension (65.0%), diabetes (33.4%), hyperlipidemia (35.2%), obesity (23.0%), and smoking history (35.8%). We observed no statistically significant differences in basic patient characteristics among the five groups except for sex (male) and diabetes.

Quantitative Coronary Angiography Results

According to the QCA analysis results, the proportions of patients without CAD, non-obstructive CAD, obstructive CAD, and severe obstructive CAD were 13.7% (62/452), 11.7% (53/452), 74.6% (337/452), and 57.1% (258/452), respectively. The proportions of lesions with at least one diameter reduction ≥50% involving the left main coronary artery, left anterior descending coronary artery, left circumflex coronary artery, right coronary artery, and isolated coronary artery branch were 4.9% (22/452), 57.1% (258/452), 33.6% (152/452), 36.9%, (167/452), and 32.3% (146/452), respectively. The proportions of one-vessel disease, two-vessel disease, three-vessel disease, left main + two-vessel disease, and left main + three-vessel disease were 24.8% (112/452), 22.1% (100/452), 19.5% (88/452), 1.5% (7/452), and 2.7% (12/452), respectively.

Diagnostic Performance Evaluation

When the cut-off value for coronary artery diameter stenosis was 50% (Table 2), the sensitivity, specificity, PPV, NPV, and accuracy of the acoustic analysis method were 81.9% (95% CI 77.4–85.9), 70.4% (95% CI 61.2–78.6), 89.0% (95% CI 85.9–91.5), 57.0% (95% CI 50.7–63.2), and 79.0% (95% CI 74.9–82.6), respectively, and the AUC value was 0.762 (95% CI 0.720–0.800). The sensitivity of the acoustic analysis method was 75.6% (95% CI 71.1–79.8), 83.3% (95% CI 78.2–87.7), and 85.7% (95% CI 78.1–91.5) when the cut-off values were 30%, 70%, and 90%, respectively. The specificity was 75.8% (95% CI 63.3–85.8), 51.0% (95% CI 43.8–58.3), and 37.5% (95% CI 32.3–43.0), respectively. The PPV was 95.2% (95% CI 92.7–96.8), 69.4% (95% CI 66.0–72.5), and 32.9% (95% CI 30.5–35.4), respectively. The NPV was 33.1% (95% CI 28.3–38.2), 69.7% (95% CI 62.9–75.8), and 88.0% (95% CI 82.3–92.1), respectively. The accuracy was 75.7% (95% CI 71.4–79.6), 69.5% (95% CI 65.0–73.7), and 50.2% (95% CI 45.5–54.9), respectively.

Table 1 Basic Patient Characteristics (n=452).

Characteristic	All (n=452)	Maximum stenosis in any vessel (excluding coronary vessels with original diameter <2.5 mm)					P value*
		<30% (n=62)	30–49% (n=53)	50–69% (n=79)	70–89% (n=139)	≥90% (n=119)	
Age (years, $\bar{x}\pm s$)	61.1±10.0	58.7±10.0	62.4±9.3	60.6±8.3	61.6±10.4	61.3±10.9	0.309
Male (%)	308 (68.1%)	30 (48.4%)	30 (56.6%)	54 (68.4%)	101 (72.7%)	93 (78.2%)	<0.001
BMI (kg/m^2, $\bar{x}\pm s$)	25.6±3.8	24.6±3.4	26.1±3.2	25.5±4.3	25.7±3.6	26.0±4.0	0.142
Hemoglobin (g/L, $\bar{x}\pm s$)	137.9±17.9	137.9±16.3	132.9±26.6	136.0±16.0	138.2±18.2	141.2±13.8	0.059
Platelets (×10^9/L, $\bar{x}\pm s$)	220.2±60.5	217.4±62.3	215.7±80.1	220.9±57.3	222.7±58.6	220.4±54.4	0.955
LVEF (%)	53.5±19.6	53.3±19.2	59.7±12.8	53.5±20.6	53.1±20.5	51.4±20.2	0.700
Hypertension (%)	294 (65.0%)	30 (48.4%)	35 (66.0%)	55 (69.6%)	92 (66.2%)	82 (68.9%)	0.057
Diabetes (%)	151 (33.4%)	6 (9.7%)	13 (24.5%)	31 (39.2%)	55 (39.6%)	46 (38.7%)	<0.001
Hyperlipidemia (%)	159 (35.2%)	20 (32.3%)	19 (35.8%)	25 (31.6%)	56 (40.3%)	39 (32.8%)	0.634
Obesity[a] (%)	104 (23.0%)	11 (17.7%)	14 (26.4%)	13 (16.5%)	36 (25.9%)	30 (25.2%)	0.379
Smoking (%)	162 (35.8%)	15 (24.2%)	19 (35.8%)	25 (31.6%)	54 (38.8%)	49 (41.2%)	0.174
Family history of CAD (%)	65 (14.4%)	6 (9.7%)	8 (15.1%)	12 (15.2%)	21 (15.1%)	18 (15.1%)	0.748

Values are mean±standard deviation, median (25th, 75th percentile) or n (%).
*Statistical differences among stenosis <30%, stenosis 30–49%, stenosis 50–69%, stenosis 70–89%, and stenosis ≥90% were determined according to analysis of variance. Red color indicates significant differences between groups. [a]BMI ≥28 kg/m^2. BMI: body mass index; LVEF: left ventricular ejection fraction.

Table 2 Diagnostic Performance of Acoustic Analysis in Obstructive CAD.

Acoustic analysis result	Quantitative coronary angiography result		Total
	≥50	<50	
Diseased	276	34	310
Normal	61	81	142
Total	337	115	452

Moreover, the AUC value was 0.757 (95% CI 0.715–0.796), 0.672 (95% CI 0.626–0.715), and 0.616 (95% CI 0.570–0.661), respectively (Table 3, Figure 3).

The sensitivity of the acoustic analysis method for identifying one-vessel disease was 86.6% (95% CI 78.9–92.3) when the cut-off value was 50%. The sensitivity for identifying left anterior descending coronary artery lesions was best, at 90.7% (95% CI 81.7–96.2). The sensitivity for identifying isolated coronary artery branch lesions was 66.7% (95% CI 41.0–86.7), whereas the sensitivity for identifying three-vessel disease in the multi-vessel coronary artery lesions was better, at 82.9% (95% CI 73.4–90.1) (Table 4).

Multivariate Analysis

In the multivariate logistic regression analysis, male sex, previous diabetes, and a turbulent murmur signal were the dominant predictors of coronary artery stenosis when the cut-off values were 30% and 50%. Only the turbulent murmur signal and male sex contributed significantly to identification of coronary artery stenosis when the cut-off values were 70% and 90% in the logistic regression analysis. In addition, regardless of coronary artery diameter, the OR of the turbulent murmur signal was maximal. The OR was largest when the cut-off value was 50%. (Table 5).

Discussion

Our study indicated that our method for acoustic analysis of turbulent murmur caused by coronary artery stenosis may provide valuable information

Table 3 Diagnostic Performance of Acoustic Analysis under Different Stenosis Cut-Off Values.

	Prevalence	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
Stenosis 30%	86.3% (390/452)	75.6% (71.1–79.8)	75.8% (63.3–85.8)	95.2% (92.7–96.8)	33.1% (28.3–38.2)	75.7% (71.4–79.6)
Stenosis 50%	74.6% (337/452)	81.9% (77.4–85.9)	70.4% (61.2–78.6)	89.0% (85.9–91.5)	57.0% (50.7–63.2)	79.0% (74.9–82.6)
Stenosis 70%	57.1% (258/452)	83.3% (78.2–87.7)	51.0% (43.8–58.3)	69.4% (66.0–72.5)	69.7% (62.9–75.8)	69.5% (65.0–73.7)
Stenosis 90%	26.3% (119/452)	85.7% (78.1–91.5)	37.5% (32.3–43.0)	32.9% (30.5–35.4)	88.0% (82.3–92.1)	50.2% (45.5–54.9)

PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve.

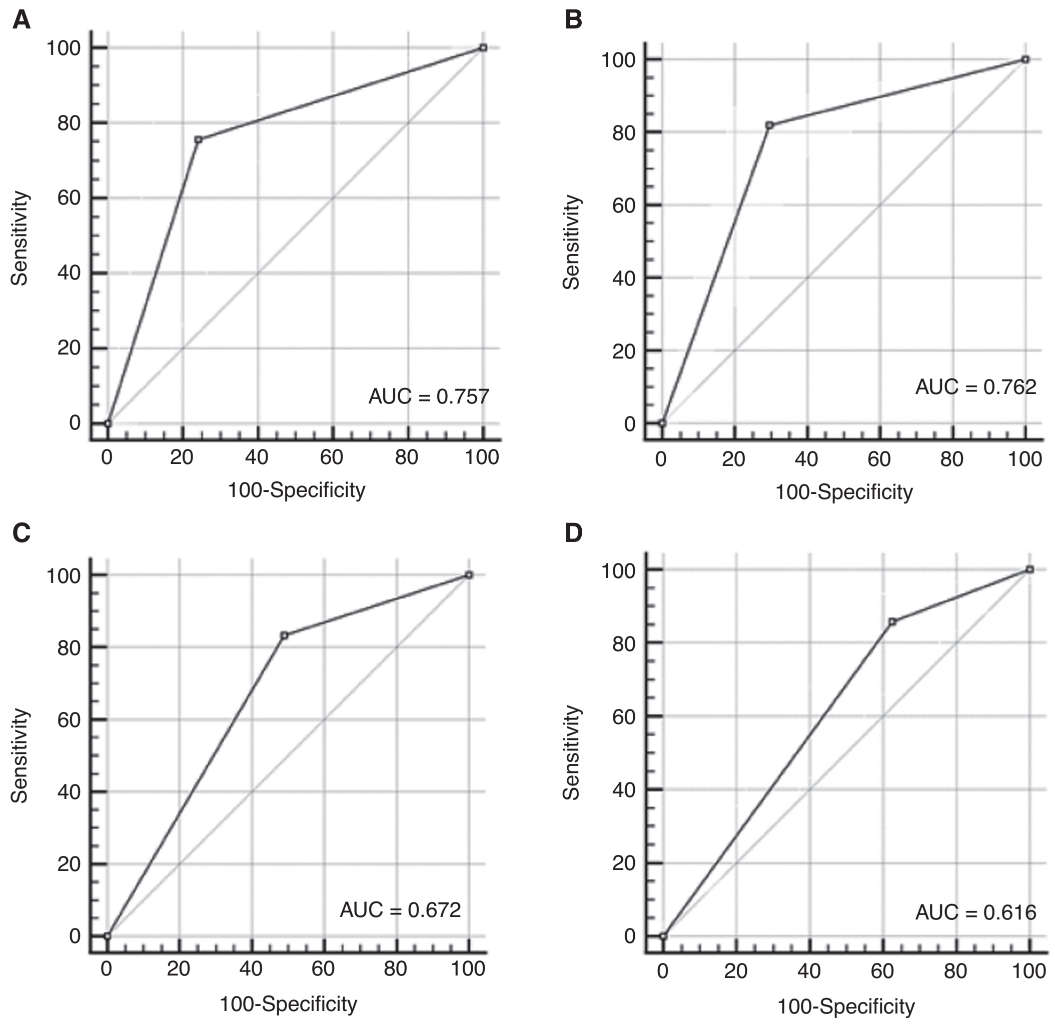

Figure 3 ROC Curves of the Diagnostic Performance of Acoustic Analysis.
AUC (A): stenosis cut-off value 30%. AUC (B): stenosis cut-off value 50%. AUC (C): stenosis cut-off value 70%. AUC (D): stenosis cut-off value 90%.

Table 4 Patients Grouped According to the Condition of Diseased Vessels (Stenosis Cut-Off Value: 50%).

	Stenosis ≥50% (n)	Acoustic analysis indicating diseased (n)	Sensitivity (95% CI)
Left anterior descending coronary artery	75	68	90.7% (81.7–96.2)
Left circumflex coronary artery	13	10	76.9% (46.2–95.0)
Right coronary artery	24	19	79.2% (57.8–92.9)
Isolated coronary artery branch	18	12	66.7% (41.0–86.7)
One-vessel disease	112	97	86.6% (78.9–92.3)
Two-vessel disease	100	81	81.0% (71.9–88.2)
Three-vessel disease	88	73	82.9% (73.4–90.1)

for CAD diagnosis in the hospitalized Chinese population. The diagnostic performance of this method differed when different degrees of coronary artery stenosis were used as cut-off values. ROC and logistic regression analysis indicated the best diagnostic performance for obstructive CAD. The sensitivity, specificity, PPV, NPV, and accuracy of the acoustic analysis method were 81.9%, 70.4%, 89.0%, 57.0%, and 79.0%, respectively, and the AUC value was 0.762. The sensitivity of the acoustic analysis method for identifying one-vessel disease was 86.6% when the cut-off value

Table 5 OR and 95% CI for the Associations between the Degree of Coronary Artery Stenosis and Possible Predictors under Different Stenosis Cut-Off Values.

Predictors	Stenosis 30%		Stenosis 50%		Stenosis 70%		Stenosis 90%	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.028 (0.995–1.062)	0.097	1.005 (0.979–1.032)	0.708	1.014 (0.992–1.037)	0.217	1.007 (0.983–1.031)	0.583
Sex (male)	2.603 (1.205–5.621)	0.015	3.550 (1.843–6.840)	<0.001	2.179 (1.310–3.624)	0.003	1.828 (1.039–3.217)	0.036
BMI	1.042 (0.957–1.136)	0.343	0.980 (0.916–1.050)	0.569	1.008 (0.952–1.068)	0.785	1.021 (0.959–1.086)	0.522
Hypertension	1.621 (0.840–3.128)	0.150	1.255 (0.724–2.175)	0.419	0.993 (0.632–1.560)	0.975	1.069 (0.658–1.738)	0.786
Diabetes	4.163 (1.637–10.588)	0.003	2.787 (1.487–5.222)	0.001	1.463 (0.933–2.294)	0.097	1.151 (0.725–1.828)	0.550
Hyperlipidemia	0.856 (0.439–1.670)	0.649	0.913 (0.531–1.570)	0.741	1.113 (0.720–1.722)	0.630	0.819 (0.513–1.305)	0.400
Smoking	1.521 (0.663–3.449)	0.325	0.907 (0.474–1.738)	0.769	1.240 (0.752–2.043)	0.400	1.128 (0.681–1.869)	0.641
Family history of CAD	1.207 (0.516–2.825)	0.655	1.313 (0.632–2.726)	0.464	1.025 (0.564–1.862)	0.935	0.777 (0.394–1.531)	0.466
Turbulent murmur signal	8.842 (4.536–17.234)	<0.001	11.027 (6.478–18.770)	<0.001	4.829 (3.077–7.576)	<0.001	3.374 (1.904–5.978)	<0.001

was 50%. The sensitivity for identifying left anterior descending coronary artery lesions was best, at 90.7%. The sensitivity for identifying isolated coronary artery branch lesions was 66.7%, whereas the sensitivity for identifying three-vessel disease in multi-vessel coronary artery lesions was better, at 82.9%.

Azimpour et al. [9] have used coronary angiography as a diagnostic criterion. Their study has indicated a sensitivity of 0.70 when the acoustic method was used to identify any coronary artery diameter stenosis ≥50%; a specificity of 0.80; and an AUC value of 0.75. The TURBULENCE [4] study, enrolling 763 participants, has used coronary CT angiography or coronary angiography to determine the presence or absence of coronary artery stenosis, and has evaluated the diagnostic performance of the acoustic method for ≥70% stenosis of major coronary arteries and ≥50% stenosis of the left main coronary artery. The sensitivity of the acoustic method was 78%, the specificity was 35%, and the AUC value was 0.582 [4].

In our study, when the cut-off value for coronary artery diameter stenosis was 50%, the sensitivity and specificity of the acoustic analysis method were 81.9% and 70.4%, and the AUC value was 0.762. When the cut-off value for coronary artery diameter stenosis was 70%, the sensitivity and specificity of the acoustic analysis method were 83.3% and 51.0%, and the AUC value was 0.672. Our findings are similar to the previously reported results.

Our study's innovation was its extensive evaluation of the potential clinical application value of the acoustic analysis method in high-risk CAD populations requiring hospitalization. Our findings may have clinical implications. The AUC values (0.757 vs. 0.762) did not change significantly when the cut-off value for coronary artery diameter stenosis was 30% versus 70%. The acoustic analysis method may be used to identify mild coronary artery stenosis lesions for early screening of CAD. Attention should be paid to patients with abnormal acoustic analysis results: other tests or assessments should be recommended, and early prevention or intervention in CAD might be suggested.

The heart sound acquisition device used herein is a modern digital electronic stethoscope with a recognizable sound frequency range of 20–2000 Hz. Its digital signal processing unit can decrease environmental noise and amplify the heart sounds signals, thereby increasing the signal-to-noise ratio [20, 21]. Several basic science studies have demonstrated that this device can be used to identify faint murmur associated with turbulent flow due to coronary artery stenosis [22, 23]. The characteristics of diastolic murmur signals associated with coronary artery stenosis in our study mainly included time domain characteristics and frequency domain characteristics, which were determined on the basis of the heart sound spectrum characteristics of 25 patients with obstructive CAD and 20 individuals without CAD in preliminary experiments, as well as the results of previous studies. However, an international consensus regarding the acoustic characteristics of turbulent murmur caused by coronary artery stenosis remains lacking [11, 19]. Differences may exist in the characteristics of acoustic signals associated with coronary artery stenosis detected by different acoustic detection equipment and/or analysis algorithms [11, 19].

Several problems remain to be solved in CAD diagnosis with the acoustic method. First, differences may exist in the characteristics of turbulent acoustic signals associated with coronary artery stenosis detected with different acoustic detection equipment and/or analytic algorithms [11, 19]. The standardization of acoustic analysis methods detecting coronary artery stenosis is a crucial problem to be solved to support clinical applications. Second, whether the acoustic analysis method further identify which vessels have stenotic lesions in CAD diagnosis remains unclear. Third, the effects of changes in participants' hemodynamic factors (including heart rate and blood pressure) on the accuracy and reproducibility of the test results during the heart sounds collection process remains to be determined. Fourth, no reports have evaluated the overall diagnostic performance of the acoustic method for one-vessel and multi-vessel lesions, different vessels, or lesions in different segments of the same vessel [11, 24]. Although our study initially evaluated the sensitivity of the acoustic analysis method for single-vessel and multi-vessel lesions, we did not assess overall diagnostic performance in different lesion types. Therefore, further research is necessary to assess the diagnostic performance of the acoustic analysis method for different lesions.

Several limitations of our study should be noted. First, the enrolled participants were inpatients, not outpatient or community patients. Because patients with comorbidities (such as atrial fibrillation, valvular heart disease, or chronic obstructive pulmonary disease) were excluded, the findings may not reflect the broader population. Second, an international consensus has yet to be reached regarding the characteristics of acoustic signals associated with coronary artery stenosis, because of differences in acoustic detection equipment and analysis algorithms. The acoustic features selected in our study might not adequately reflect coronary artery lesions. However, the results of our study suggest that the acoustic analysis method may have value in CAD diagnosis. Third, this study is a small sample and single-center study. In the future, the sample size must be expanded, and multi-center studies must be performed to explore the clinical application value of this new detection method.

In conclusion, the acoustic analysis method of turbulent murmur caused by coronary artery stenosis may have value in CAD diagnosis in the Chinese population. It has good diagnostic performance for CAD when the cut-off value for coronary artery diameter stenosis is 50%. The acoustic analysis method for CAD diagnosis has advantages of low cost, safety, and an absence of radiation. It may be used as a new detection technology to enrich the current non-invasive detection methods for CAD.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Ethics Approval and Consent to Participate

This study involving human participants was reviewed and approved by the Ethics Committee of the Sixth Medical Center of People's Liberation Army General Hospital (No. HZKY-PJ-2021-21). All participants provided signed informed consent.

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