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ARTICLE

Diagnostic value of multimodal cardiovascular imaging technology coupled with biomarker detection in elderly patients with coronary heart disease

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Abstract

Aims/Background Coronary heart disease is a common disease in the elderly and has a complex pathogenesis, which complicates the clinical diagnostic process. Thus, enhancing the diagnostic efficiency for coronary heart disease is imperative to improve the life expectancy of the elderly. This study aimed to explore the diagnostic value of multimodal cardiovascular imaging technology coupled with biomarker detection in elderly patients with coronary heart disease.

Methods The medical records of 421 patients with suspected coronary heart disease obtained from the geriatric department of the First Affiliated Hospital of Hebei North University from February 2020 to February 2023 were retrospectively analysed. After excluding 10 patients who did not meet the inclusion criteria, the remaining 411 patients were included in this study. The included subjects had undergone coronary computed tomography angiography and were divided into coronary heart disease group (n=208) and non-coronary heart disease group (n=203) according to the diagnostic results. Multimodal cardiovascular imaging (coronary computed tomography angiography and echocardiography) and detection of serum biomarkers such as small dense low-density lipoprotein, lipoprotein a, and gamma-glutamyl transferase were performed in both groups. The clinical indicators of the two groups were compared, and the combined diagnostic efficacy of multimodal cardiovascular imaging and biomarker detection was evaluated.

Results Compared to the non-coronary heart disease group, the coronary heart disease group had significantly higher levels of maximum area stenosis, total plaque volume, total plaque burden and fibrotic plaque volume ($p < 0.001$), and lower left ventricular ejection fraction level ($p < 0.001$). Additionally, the coronary heart disease group exhibited higher levels of left ventricular end-diastolic volume, left ventricular end-systolic volume and stroke volume than the non-coronary heart disease group ($p < 0.001$), and had higher levels of small dense low-density lipoprotein, lipoprotein a and gamma-glutamyl transferase ($p < 0.001$). Our results demonstrated that combined diagnosis had better diagnostic efficacy than individual approaches, marked by higher area under the curve and sensitivity of the former ($p < 0.001$).

Conclusion Multimodal cardiovascular imaging technology combined with biomarker detection can distinctly improve the accuracy of coronary heart disease diagnosis in elderly patients.

Key words: Biomarkers; Coronary heart disease; Diagnosis; Multimodal cardiovascular imaging technology

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Introduction

Coronary heart disease (CHD) has emerged as a global health problem following the significant improvement in living standards. The number of patients with cardiovascular disease in China has exceeded 290 million, including 11 million patients with CHD (Tian et al, 2019). The CHD is showing a steadily increasing trend in incidence, representing a

huge challenge to the health of the elderly population. Of note, the incidence of CHD is also on the rise in the younger populations (Hong et al, 2023; Zhang et al, 2023). Given the far-reaching clinical impacts of CHD, it is exigent to devise an approach that can efficiently and effectively predict the occurrence of CHD in individuals with an increased risk for the disease. Coronary computed tomography angiography (CCTA) is regarded as the gold-standard detection tool for CHD, which can accurately evaluate the structural changes and stenosis of coronary vessels. However, CCTA is a high-cost, invasive technique, which compared to non-invasive options, is a lacklustre detection technique in clinical settings (Li M et al, 2023).

Since the mid-1990s, a gradual exploration of medical imaging fusion technology has started, leading to its widespread investigation and rapid technological development. Multimodal cardiovascular imaging technology is a nascent diagnostic technique combining different imaging modalities for use in the detection of cardiovascular diseases. This hybrid technology aids in the diagnosis of cardiovascular diseases by leveraging and accentuating the features exhibited in images stemming from different imaging modes. In detail, multimodal cardiovascular imaging combines anatomical, morphological and functional data obtained through various non-invasive imaging techniques to provide accurate diagnostic and prognostic information regarding CHD (Chen et al, 2019). In fact, a multimodality-based diagnostic model is commonly utilised in the management of CHD, but achieving early diagnosis proves to be challenging due to the lack of specific biomarkers (Chen et al, 2023). Therefore, it is necessary to find reliable biomarkers that can improve the early diagnosis of CHD. Through years of discovery and investigation, several biomarkers were found to demonstrate a potential for CHD diagnosis. For instance, small dense low-density lipoprotein (sd-LDL) is considered an emerging risk factor for atherosclerotic cardiovascular disease and a promising marker of cardiovascular disease (Kanonidou, 2021). Lipoprotein a (Lpa) is a cholesterol-like particle, and its elevated level is an independent and heritable risk factor for atherosclerotic heart disease (Lampsas et al, 2023). The gamma-glutamyl transferase (γ-GGT) may be an inflammatory marker, which is an additional indicator for assessing cardiovascular risk (He et al, 2023). At present, reports on the application of multimodal cardiovascular imaging technology coupled with biomarker detection in the diagnosis of CHD remain scarce. Thus, a retrospective analysis was conducted to explore the diagnostic efficacy of such a fusion technique for CHD patients.

Methods

Study participants

A total of 421 elderly patients with suspected CHD in the First Affiliated Hospital of Hebei North University from February 2020 to February 2023 were selected for this retrospective analysis. After excluding 10 patients who did not meet the inclusion criteria, the remaining 411 patients were included in this study. All research subjects had undergone CCTA and were divided into the CHD group (n=208) and non-CHD group (n=203) according to the diagnostic results. The patients' baseline data are shown in Table 1. The study was conducted in line with the principles set out in the Declaration of Helsinki (2013) (World Medical Association, 2013).

Inclusion and exclusion criteria

Only individuals meeting the inclusion criteria in the following were included in this study: (1) patients with complete clinical data; (2) patients without mental disorders; and (3) patients over 60 years old.

Study participants who have the pathological conditions mentioned in the following were excluded: (1) patients with liver, lung and kidney dysfunction; (2) patients with malignant tumours; and (3) patients with severe infectious diseases, such as viral hepatitis and syphilis.

Detection methods

The data utilised in this study were collected from the electronic medical records of the hospital. The attending physicians who examined the patients and administered or

Table 1. Comparison of baseline data between coronary heart disease and non-coronary heart disease groups

	CHD group (*n*=203)	Non-CHD group (*n*=208)	X^2/z	*p*
Gender			0.358	0.549
Male	124 (61.08)	133 (63.94)		
Female	79 (38.92)	75 (36.06)		
Age (years old, M [P_{25}, P_{75}])	73.00 (66.00, 81.00)	73.00 (67.00, 80.00)	–0.229	0.819
BMI (kg/m^2, M [P_{25}, P_{75}])	21.10 (19.50, 23.80)	21.35 (19.10, 23.68)	–0.616	0.538
Underlying diseases				
Hypertension	130 (64.04)	135 (64.90)	0.034	0.855
Diabetes	117 (57.64)	109 (52.40)	1.136	0.286
Residence			0.666	0.415
City	109 (53.69)	120 (57.69)		
Countryside	94 (46.31)	88 (42.31)		
Smoking history			0.362	0.548
Yes	79 (38.92)	87 (41.83)		
No	124 (61.08)	121 (58.17)		
Drinking history			0.727	0.394
Yes	92 (45.32)	103 (49.52)		
No	111 (54.68)	105 (50.48)		
Educational level			0.402	0.982
Bachelor degree and above	5 (2.46)	4 (1.92)		
Junior college education	22 (10.84)	25 (12.02)		
High school diploma	49 (24.14)	52 (25.00)		
Junior high school diploma	86 (42.36)	84 (40.38)		
Primary school diploma and below	41 (20.20)	43 (20.67)		

Note: CHD, coronary heart disease; BMI, body mass index.

prescribed the diagnostic tests were interviewed. The detection methods are summarised in the following:

1. In this study, 5 mL of fasting venous blood was collected from all study participants after admission and centrifuged at 3000 r/min for 10 min. Serum Lpa level was detected using a double-antibody sandwich enzyme-linked immunosorbent assay (CS11862, Shanghai Fusheng Industrial Co., Ltd., Shanghai, China), and serum sd-LDL level was measured using peroxidase method (KMEOt010299, Whenzhou KeMiao Biological Technology Co., Ltd., Wenzhou, China). The procedures were followed in strict accordance with the manufacturers' instructions. An automatic biochemical analyser (GRT-300, Jinan Glite Technology Co., Ltd., Jinan, China) was used to determine the γ-GGT level.
2. All patients underwent the conventional CCTA scan using a 320-row CT volume scanner (Aquilion ONE GENESIS, Canon, Tokyo, Japan). Cardiac function analysis was added to the examination to evaluate the condition of coronary artery. During the examination, patients were laid in the supine position. The scanning range was 16 cm, from 1 cm below the tracheal carina to the bottom of the heart. Tube voltage was set as 100–120 kV; tube current was automatic; and collimation of detector was set as 320 × 0.5 mm. All subjects were scanned with a retrospective electrocardiogram gating technique for at

least one cardiac cycle. An 18G venous indwelling needle was embedded in the elbow vein of patients. Non-ionic contrast agent iopromide (70–100 mL; Ultravist, 320 mgI/mL) was injected at a rate of 4–6 mL/s, and 30 mL of normal saline was injected at 5.0 mL/s in a double-channel high-pressured syringe. Image processing was performed by experienced radiologists. Ten sets of images were reconstructed from the original data at a 10% interval, then the reconstructed data were input into the workstation (Vitrea Advanced, Toshiba Corporation, Tokyo, Japan). The best phase of coronary artery display was selected to reconstruct the coronary artery, and the image of each group was post-processed using a specific cardiac function analysis software in the workstation. The maximum area stenosis (MAS), total plaque volume (TPV), total plaque burden (TPB) and fibrotic plaque volume (FPV) were calculated by the Agatston algorithm. Coronary heart disease is diagnosed based on the MAS findings: patients with a score <50% are diagnosed with coronary atherosclerosis instead of CHD; those with 50%–70% are diagnosed with possible CHD, characterised by a borderline lesion that necessitates further examination; and those with >70% are diagnosed with CHD.

3. The colour Doppler ultrasound diagnostic instrument (Aplio i900, Canon Company, Tokyo, Japan) was adopted for echocardiographic detection in patients with CHD, with a probe frequency of 2.5 MHz. The patients were placed in a left lateral position, and the probe was placed three to five ribs apart on the left side of the sternum. The parasternal long-axis view and subxiphoid four chamber section were selected. The size of the heart chamber, the diameter of blood vessels, the thickness of the valve, the amplitude in motion and coordination of the ventricular wall, and the echo intensity of the myocardium were observed. The left ventricular end-diastolic and end-systolic diameters were measured. Left ventricular ejection fraction (LVEF, normal range: 50%–70%), left ventricular end-diastolic volume (LVEDV, normal range: 108–132 mL), left ventricular end-systolic volume (LVESV, normal range: 29–61 mL) and stroke volume (SV, normal range: 60–80 mL) were measured three times by the system to calculate the average value (Saraste and Knuuti, 2020).

Statistical analysis

SPSS version 26.0 (International Business Machines Corporation, Armonk, NY, USA) was used to analyse and process the data in this study. Categorical variables such as underlying disease, residence, smoking history, drinking history and education level are presented as counts and percentages, and analysed using the Chi-squared test. The data normality of continuous variables was assessed using Kolmogorov-Smirnov method. Continuous variables with non-normal distribution, including age, body mass index, parameters of CCTA and echocardiography, sd-LDL, Lpa and γ-GGT, are expressed as the median and interquartile range (M [P_{25}, P_{75}]). Mann-Whitney *U* test was employed to compare the data between groups. The diagnostic efficacy of combined as well as individual approaches was evaluated by means of the receiver operating characteristic (ROC) curve. A difference was considered statistically significant if $p < 0.05$.

Results

Comparison of coronary computed tomography angiography parameters

The imaging results showed that the CHD group had significantly higher levels of MAS, TPV, TPB and FPV than the non-CHD group ($p < 0.05$), as detailed in Table 2.

Comparison of echocardiographic parameters

Compared to the non-CHD group, the CHD group had lower LVEF level ($p < 0.001$), and higher levels of LVEDV, LVESV and SV ($p < 0.001$), as detailed in Table 3.

Comparison of biomarkers levels

The CHD group had higher levels of sd-LDL, Lpa and γ-GGT than the non-CHD group ($p < 0.001$), as detailed in Table 4.

Table 2. Comparison of coronary computed tomography angiography parameters between coronary heart disease and non-coronary heart disease groups

Groups	MAS (%)	TPV (mm^3)	TPB (%)	FPV (mm^3)
CHD group (n=203)	81.00 (69.00, 89.00)	126.00 (105.00, 165.00)	71.00 (67.00, 78.00)	92.00 (82.00, 99.00)
Non-CHD group (n=208)	64.00 (56.00, 75.00)	101.00 (92.00, 109.00)	67.00 (61.00, 73.00)	77.00 (69.00, 85.00)
z	–2.823	–7.891	–5.256	–8.089
p	0.005	<0.001	<0.001	<0.001

Note: Data are expressed as median and interquartile range (M [P_{25}, P_{75}]). CHD, coronary heart disease; MAS, maximum area stenosis; TPV, total plaque volume; TPB, total plaque burden; FPV, fibrotic plaque volume.

Table 3. Comparison of echocardiographic parameters between coronary heart disease and non-coronary heart disease groups

Groups	LVEF (%)	LVEDV (mL)	LVESV (mL)	SV (mL)
CHD group (n=203)	38.00 (34.00, 53.00)	151.00 (132.00, 166.00)	50.00 (38.00, 62.00)	65.00 (59.00, 70.00)
Non-CHD group (n=208)	57.00 (39.25, 64.00)	124.00 (114.00, 146.75)	39.00 (31.25, 48.75)	60.00 (55.00, 63.00)
z	–7.900	–7.523	–6.028	–7.639
p	<0.001	<0.001	<0.001	<0.001

Note: Data are expressed as median and interquartile range (M [P_{25}, P_{75}]). CHD, coronary heart disease; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; SV, stroke volume.

Table 4. Comparison of small dense low-density lipoprotein, lipoprotein a and gamma-glutamyl transferase levels between coronary heart disease and non-coronary heart disease groups

Groups	sd-LDL (mmol/L)	Lpa (mmol/L)	γ-GGT (U/L)
CHD group (n=203)	1.35 (0.50, 1.56)	111.00 (82.00, 125.00)	58.84 (34.33, 66.03)
Non-CHD group (n=208)	0.50 (0.49, 1.40)	83.00 (76.00, 105.75)	36.14 (26.54, 59.86)
z	–5.981	–5.972	–5.608
p	<0.001	<0.001	<0.001

Note: Data are expressed as median and interquartile range (M [P_{25}, P_{75}]). CHD, coronary heart disease; sd-LDL, small dense low-density lipoprotein; Lpa, lipoprotein a; γ-GGT, gamma-glutamyl transferase.

Diagnostic efficacy analysis of multimodal cardiovascular imaging technology, biomarker detection and the combined diagnosis

The hybrid detection approach combining multimodal cardiovascular imaging technology and biomarker detection manifested higher efficacy in CHD diagnosis than its component techniques, evidenced by higher area under the ROC curve (AUC) in the former ($p < 0.001$), as detailed in Table 5 and Figure 1.

Discussion

As a major public health problem, cardiovascular disease poses a huge social and economic burden in the world's healthcare arena (Tikkanen et al, 2018). Compared with their younger counterparts, elderly patients suffer from a more severe form of CHD (Zhen et al, 2022). Since treatments for early-stage CHD have higher curative effects, it is of high clinical significance to identify the disease in the early phase to elevate the chances of recovery. Coronary angiography is the gold-standard diagnostic approach for CHD, but the invasive

Table 5. Comparison of clinical diagnostic efficacy of different diagnostic methods

	AUC	Standard error	95% CI		Sensitivity (%)	Specificity (%)	*p*
			Lower limit	Upper limit			
Multimodal cardiovascular imaging technology	0.793	0.022	0.749	0.837	0.675	0.827	<0.001
Serum biomarker detection	0.668	0.027	0.616	0.721	0.660	0.678	<0.001
Combined diagnosis	0.808	0.021	0.766	0.851	0.675	0.837	<0.001

Abbreviations: AUC, area under the ROC curve; CI, confidence interval.

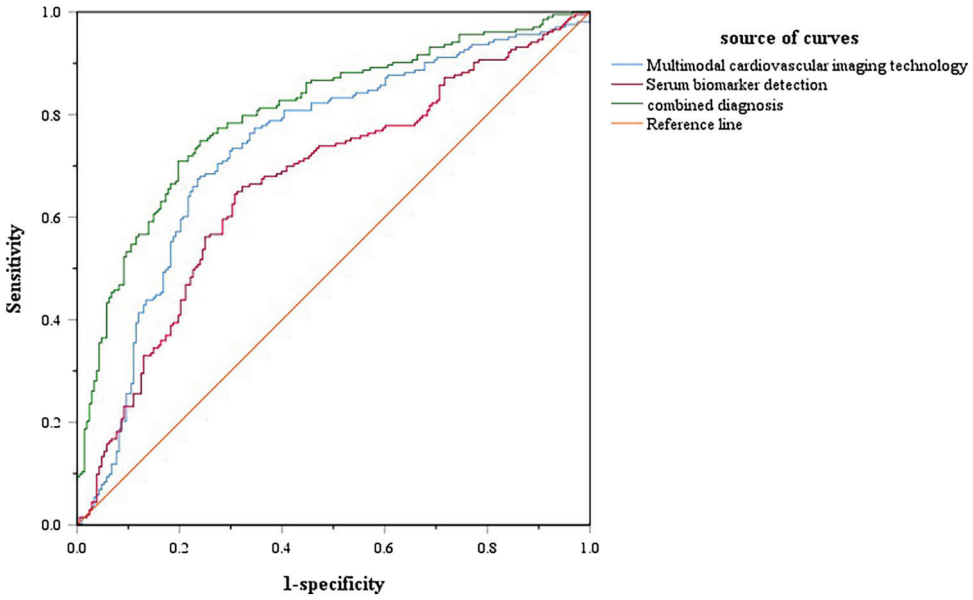

Figure 1. Receiver operating characteristic curves of combined and individual approaches used in coronary heart disease detection.

mode has limited the wide adoption of this method and thus driven the efforts to develop non-invasive and efficient options.

Multimodal cardiovascular imaging technology refers to the imaging technology that combines multiple imaging technologies and integrates the processing of images obtained from different modes of detection (Evangelista et al, 2023). This technique provides a wide range of information to help with cardiovascular disease diagnosis, addressing the complexities and limitations inherent in the clinical assessment of this kind of disease (Cardim et al, 2015). This hybrid intravascular imaging technology, combining the advantages of different imaging modalities, offers a comprehensive assessment of cardiovascular disease by evaluating plaque morphology, delineating pathobiology and predicting evolution of lesions (Mushenkova et al, 2020).

The rapid advances of molecular biology techniques in recent decades have led to the discovery of a plethora of biomarkers, which play an important role in the diagnosis and treatment of various diseases. Due to the difficulty in clinical diagnosis and treatment of CHD, it is of utmost importance to find reliable biomarkers. Numerous studies have been conducted to explore the pathogenesis of CHD, shedding light on pathways centred on oxidative stress, inflammation and lipids. Arenas de Larriva et al (2020) pointed out that oxidative stress plays a central role in the occurrence and maintenance of cardiovascular disease. A study by Ostadmohammadi et al (2022) revealed that inflammatory response increases the incidence of CHD. Additionally, Marzoog (2023) showed that abnormal blood

lipid levels can heighten cardiovascular risk. These prior findings indicate that biomarkers of blood lipid and inflammatory response can facilitate the diagnosis of CHD.

1. Blood lipid markers. Low-density lipoprotein (LDL) is the main carrier of cholesterol, and can be modified to oxidised low-density lipoprotein (ox-LDL) under oxidative stress. ox-LDL is a strong ligand for macrophages, which phagocytise ox-LDL through their scavenger receptors. The accumulation of ox-LDL in macrophages produces a morphological appearance of soap bubbles and leads the macrophages to become foam cells, which subsequently cause atherosclerotic lesions, accumulation of atherosclerotic plaques, and restriction of blood flow to the myocardium (Khatana et al, 2020). Small dense low-density lipoprotein is a sub-component with small particles and high density in LDL. A growing line of evidence supports sd-LDL as a marker of cardiovascular disease. Other studies have shown that the sd-LDL level reduction can overtly decrease the incidence of cardiovascular disease (Pradhan et al, 2022; Yanai et al, 2022). Lipoprotein a is a compound of apolipoprotein a and LDL in the liver. Elevated levels of Lpa are an independent and heritable risk factor for atherosclerotic cardiovascular disease (Kronenberg et al, 2022). Lipoprotein a is the preferred protein carrier of oxidised phospholipids, which has an effect on vascular inflammation, atherosclerotic lesions, endothelial function and thrombosis, leading to cardiovascular disease (Ndrepepa et al, 2018).
2. Inflammatory response markers. Gamma-glutamyl transferase is a ubiquitous enzyme that generates glutathione or other γ-glutamyl compounds. Glutathione represents a class of the most important antioxidant in human cells, and γ-GGT plays an important role in maintaining the stability and metabolism of glutathione, which acts in defending against oxidative stress (Ndrepepa et al, 2018). Elevated γ-GGT levels can cause abnormal lipid metabolism, reduced lipid peroxidation, release of inflammatory factors, and vascular endothelial damage, affect stability of plaque, cause the damage and enlargement of plaque, and induce acute coronary syndrome (Chen J et al, 2024).

As a measure of disease diagnosis efficacy, the AUC value is commonly used to evaluate the newly developed diagnostic model. In practice, a value closer to 1 indicates better diagnostic efficacy. In this study, the AUC value of the combined diagnosis was higher than that of the individual techniques. Thus, the merging of multimodal cardiovascular imaging technology with the detection of serum sd-LDL, Lpa and γ-GGT levels can make up for the deficiency of single-dimension detection, providing a more reliable basis for clinical diagnosis and treatment of CHD in elderly patients.

However, this study has several limitations. Due to the constraints in time, funding and manpower, this study had a relatively small sample size. Also, the patients were recruited from a single centre. Therefore, the results of the current study cannot be generalised to other populations. Limited by the research conditions, the study applied echocardiography, which is not a highly effective method for CHD diagnosis, to detect the condition and differentiate the included participants.

Conclusion

In summary, the combined application of multimodal cardiovascular imaging technology and biomarker detection provides an efficient avenue for CHD diagnosis.

Key points

- The levels of maximum area stenosis, TPV, TPB and FPV in the CHD group were significantly higher than those in the non-CHD group.
- Compared to the non-CHD group, the CHD group had lower left ventricular ejection fraction levels and higher levels of LVEDV, LVESV and SV.
- The CHD group had higher levels of small dense low-density lipoprotein, lipoprotein a, and gamma-glutamyl transferase than the non-CHD group.
- Featuring higher AUC and sensitivity, the combined diagnosis boasts higher diagnostic efficacy than the individual component techniques.

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Availability of data and materials

The datasets used and analyzed during the current study were available from the corresponding author upon reasonable request.

Author contributions

XCL and YL designed the study. WTL and YTZ conducted the study. WTL, YTZ, FY, YXZ, SLZ and YQM collected and analyzed the data. FY and YXZ participated in drafting the manuscript, and all authors contributed to the critical revision of the manuscript for important intellectual content. All authors gave final approval of the version to be published. All authors participated fully in the work, take public responsibility for appropriate portions of the content, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics approval and informed consent

This study has been approved by the ethics committee of the First Affiliated Hospital of Hebei North University (approval No.: K2021088). All patients included in this study had informed consent and signed relevant agreements.

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Conflict of interest

The authors declare no conflict of interest.

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