Observational Study

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Risk factors and major adverse cardiovascular events of isolated coronary artery ectasia

An observational study

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Abstract

To evaluate the cardiac index and major adverse cardiovascular events (MACE) events between isolated coronary artery ectasia (CAE) and control groups over 1 year period from diagnosis. A total of 18 patients who were diagnosed with isolated CAE in the Second Hospital of Hebei Medical University from December 2020 to December 2021 were included in CAE group. About 36 patients with non-obstructive coronary artery lesions were included in the control group. All patients in 2 groups completed dobutamine stress echocardiography (DSE) during hospitalization. The chamber size, wall thickness, left ventricular ejection fraction, and left ventricular diastolic function indicators (including E/A ratio, e', and E/e' ratio) were measured. MACE and all-cause death were measured during follow-up after discharge. Interventricular septum thickness (IVSd), left ventricular posterior wall (LVPW) thickness in diastole and E/e' in CAE group were significantly higher than control group ($P < .05$). No significant differences were found in prognosis including angina, myocardial ischemia (MI), patient readmission and cardiovascular death ($P > .05$). In CAE group, coronary angiography showed dilation of left anterior descending (LAD) in 1 case, left circumflex (LCX) in 3 cases and right coronary artery (RCA) in 14 cases. Multivariate logistic regression analysis showed that BMI and IVSd were independent risk factors for CAE. IVSd, LVPW thickness in diastole and E/e' in CAE group were significantly higher than control group. BMI and IVSd were independent risk factors for isolated CAE, and had a good predictive value for isolated CAE.

Abbreviations: ACS = acute coronary syndrome, CAE = coronary artery ectasia, DSE = dobutamine stress echocardiography, IVSd = interventricular septum, LAD = left anterior descending, LCX = left circumflex, LVPW = left ventricular posterior wall, MACE = major adverse cardiovascular events, MCE = myocardial contrast-enhanced echocardiography, MI = myocardial ischemia, RCA = right coronary artery, ROC = receiver operating characteristic, SD = standard deviation.

Keywords: dobutamine stress echocardiography, interventricular septum thickness, isolated coronary artery ectasia, major adverse cardiovascular events, risk

1. Introduction

Coronary artery ectasia (CAE) is a rare but well-recognized anatomical abnormality of the coronary arteries.[1] Generally, it refers to the diffuse dilation of one or more subepicardial coronary arteries, which exceeds 1.5 times of the adjacent normal segment, and the local dilation of more than 2 times is generally called coronary aneurysm.[2,3] Isolated CAE, in absence of atherosclerosis, coronary stenosis, and other heart diseases, is very rare with an angiographic frequency of 0.1% to 0.32%.[4] Myocardial infarction can occur as a result of segmental dilatation of a coronary artery or thrombotic occlusion of a dilated vessel.[5] Due to the low detection rate of CAE, there is a lack of understanding of its etiology, risk factors, pathogenesis, pathophysiology, epidemiology, clinical manifestations, treatment options, and long-term prognosis, and it is prone to the risk of adverse cardiovascular events.[6]

Myocardial contrast-enhanced echocardiography (MCE) is a new ultrasound technology that has been gradually applied in

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

The study was approved by the Ethics Committee of the Second Hospital of Hebei Medical University (2020-R346). Written informed consent was obtained from the patients or a legal representative.

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clinical practice in recent years, which can display the perfusion of myocardial microcirculation in real-time.[7] Dobutamine stress echocardiography (DSE) induces myocardial ischemia (MI) in the stenotic coronary artery supply area by increasing myocardial oxygen consumption, and can detect MI that is difficult to detect by conventional echocardiography in a resting state, which is also important first-line noninvasive imaging technique for risk stratification and guiding revascularization in patients with MI.[8] However, there is a lack of prognostic evaluation methods, and risk factors for isolated CAE remain controversial. In this study, we aimed to use MCE combined with DSE to evaluate the cardiac index and follow-up on whether there are major adverse cardiovascular events (MACE) events within 1 year between the isolated CAE and control groups, and this study also aims to provide a basis for risk stratification of CAE patients.

2. Materials and methods

2.1. Patients

A total of 18 patients who were diagnosed with isolated CAE with coronary angiography due to angina pectoris in the Second Hospital of Hebei Medical University from December 2020 to December 2021 were included in CAE group. About 36 patients with non-obstructive coronary artery lesions (stenosis < 50%) were included in the control group (Control group). All patients in 2 groups also completed DSE during hospitalization.

Exclusion criteria were patients with single or multiple coronary artery obstructive lesions; with previous coronary revascularization; with acute myocardial infarction, severe valvular heart disease, severe heart failure (cardiac function grade III–IV), severe cardiomyopathy, malignant arrhythmia, and cardiogenic shock; with severe respiratory diseases; with the blood pressure ≥ 220/110 mm Hg after active treatment.

The study was approved by the Ethics Committee of the Second Hospital of Hebei Medical University (2020-R346). Written informed consent was obtained from the patients or a legal representative.

2.2. Cardiac ultrasonography

All patients routinely underwent 2-dimensional echocardiography before DSE. According to the guidelines of the American Society of Echocardiography,[9] the chamber size, wall thickness, left ventricular ejection fraction, and left ventricular diastolic function indicators (including E/A ratio, e', and E/e' ratio) were measured.

2.3. Contrast-enhanced DSE

Dobutamine was injected at an initial dose of 5 μg/kg/min and subsequently increased to 10 μg/kg/min and then 20 μg/kg/min every 3 minutes, up to 40 μg/kg/min. Atropine (≤2 mg) was given when required. Any changes in heart rate and blood pressure were observed. The DSE index included maximal age-predicted heart rate, number of persons achieving maximal age-predicted heart rate, maximal heart rate, systolic pressure, and diastolic pressure.

2.4. Coronary angiography

The results of coronary angiography were jointly reviewed by cardiologists to evaluate whether there was atherosclerosis, dilatation or obstructive lesions in the coronary arteries (coronary artery stenosis ≥ 50%). The diameters of adjacent normal vessels and dilated vessels were measured respectively. When the dilated vessel diameter exceeds 1.5 times of the adjacent normal segment, it is diagnosed as CAE; when it exceeds 2 times of the adjacent normal segment, it is diagnosed as coronary aneurysm. For the diffuse dilation of the coronary artery throughout the whole process, the corresponding vessel diameter in normal coronary angiography was used as a reference. CAE in the absence of atherosclerosis, inflammatory disease, or other congenital causes is called isolated CAE.

2.5. Prognosis of patients

MACE and all-cause death were measured during follow-up after discharge. MACE events were defined as: angina, myocardial infarction (MI), readmission, and cardiovascular death. The average follow-up time was 12 months, and all follow-up data were obtained by telephone.

2.6. Statistical analysis

All data analysis was performed using SPSS 26.0 statistical software. The numerical data were expressed using mean ± standard deviation (SD), and compared using independent sample t-tests; non-normally distributed numerical data were expressed as median (Q1, Q3), and compared using a rank-sum test. Classification data were expressed as number and percentage and compared using a χ^2 test. Univariate logistic analysis was used to analyze the related risk factors of isolated CAE. Multivariate logistic regression analysis was used to establish the logistic regression model. The receiver operating characteristic (ROC) curve was used to evaluate the diagnostic value of the logistic regression model, and $P < .05$ was considered to be statistically different.

3. Results

3.1. General data

There were significant differences in weight, BMI and drinking between the 2 groups ($P < .05$) (Table 1).

3.2. Cardiac index

*3.3.*Interventricular septum thickness (IVSd), left ventricular posterior wall (LVPW) thickness in diastole and E/e' in CAE group were significantly higher than control group ($P < .05$) (Table 2).

3.3. Comparison of heart rate and blood pressure

There were no significant differences in maximal age-predicted heart rate, number of persons achieving maximal age-predicted heart rate, maximal heart rate, systolic pressure and diastolic pressure between 2 groups ($P > .05$) (Table 3).

3.4. Comparison of prognosis

No significant differences were found in prognosis including angina, MI, patient readmission and cardiovascular death ($P > .05$) (Table 4).

Table 1

Comparison of general data.

Variables	CAE group (n = 18)	Control group (n = 36)	*P*
Male, n (%)	9 (50.00%)	14 (38.89%)	.436
Age	57.61 ± 9.56	59.36 ± 9.99	.541
Height	168.06 ± 9.55	166.58 ± 8.35	.563
Weight	76.17 ± 12.66	68.68 ± 10.22	.023
BMI	27.64 ± 4.25	24.77 ± 3.32	.009
Smoking, n (%)	8 (44.44%)	9 (25.00%)	.147
Drinking, n (%)	9 (50.00%)	7 (19.44%)	.020

CAE = coronary artery ectasia.

Table 2

Comparison of cardiac index.

Variables	CAE group (n = 18)	Control group (n = 36)	*P*
E/A	0.80 (0.70, 1.20)	0.70 (0.70, 0.80)	.109
EF%	63.80 (60.625, 66.15)	65.65 (62.43, 67.58)	.359
IVS	10.00 (9.00, 11.25)	9.00 (8.25, 10.00)	.002
LVPW	10.00 (9.00, 11.00)	9.00 (8.25, 10.00)	.006
LA	34.50 (32.75, 35.75)	33.00 (30.25, 35.00)	.143
LV	47.00 (45.25, 50.00)	46.00 (43.00, 48.00)	.099
RA	33.00 (29.75, 35.25)	30.00 (28.25, 33.75)	.105
RV	21.50 (19.75, 23.00)	21.00 (20.00, 22.00)	.780
e'	6.00 (4.75, 7.00)	6.00 (5.00, 7.00)	.400
E/e'	12.00 (9.94, 14.36)	10.60 (9.22, 11.90)	.045
Abnormal DSE, n (%)	5 (27.78%)	9 (25.00%)	.826

DSE = dobutamine stress echocardiography, IVS = interventricular septum, LA = left atrial, LV = left ventricular, LVPW = left ventricular posterior wall, RA = right atrial, RV = right ventricular.

Table 3

Comparison of heart rate and blood pressure.

Variables	CAE group (n = 18)	Control group (n = 36)	*P*
Maximal age-predicted heart rate	161.89 ± 8.818	159.25 ± 10.793	.374
Number of persons achieving maximal age-predicted heart rate	95.00 (90.75, 100.00)	94.00 (91.00, 97.50)	.471
Maximal heart rate	154.61 ± 10.733	150.28 ± 12.337	.210
Systolic pressure	193.17 ± 9.775	189.86 ± 12.357	.327
Diastolic pressure	103.50 (101.75, 105.00)	104.00 (102.00, 107.75)	.338

Table 4

Comparison of prognosis.

Variables	CAE group (n = 18)	Control group (n = 36)	*P*
Angina	0	2 (5.56%)	.440
MI	0	0	—
Patient readmission	1 (5.56%)	0	.333
Cardiovascular death	0	0	—

MI = myocardial infarction.

Table 5

The distribution of dilation in CAE.

Variables	Cases
LAD	1
LCX	3
RCA	14

LAD = left anterior descending, LCX = left circumflex, RCA = right coronary artery.

3.5. Distribution of dilation

In CAE group, coronary angiography showed dilation of left anterior descending (LAD) in 1 case, left circumflex (LCX) in 3 cases and right coronary artery (RCA) in 14 cases (Table 5).

Multivariate logistic regression analysis showed that BMI and IVSd were independent risk factors for isolated CAE (Fig. 1). The ROC curve for the model consisting of all risk factors for predicting isolated CAE showed a good predictive value, with an area under the curve of 0.818 and 95% CI of 0.685 to 0.951 ($P < .001$) (Fig. 2).

4. Discussion

In this study, IVSd, LVPW thickness in diastole and E/e' in CAE group were significantly higher than control group. BMI and IVSd were independent risk factors for isolated CAE, and had a good predictive value for CAE.

Stable angina occurred in 70% patients with CAE.[10] Previous study[6] found that the extent of CAE is correlated with coronary flow velocity and clinical manifestation independent of coexisting significant coronary stenoses. In the study by Gunasekaran et al,[6] 44% of CAE patients presented with acute coronary syndrome (ACS). Isolated CAE patients with ACS as the main manifestation were significantly less than those complicated with coronary artery obstructive lesions (23% vs 60%, $P < .01$). In a study by Fuwai Hospital,[11] 48.7% of patients with isolated CAE presented with angina pectoris. Esposito et al[12] analyzed several possible causes of ACS in CAE patients, including atherosclerotic plaque instability, endoluminal thrombosis caused by blood flow disturbance and blood stasis, and distal embolization of thrombotic material. In this study, we found that about 62.5% of patients with isolated CAE showed stable angina or unstable angina, which may be related to slow coronary blood flow.

Our study found that RCA (77.78%) was the most frequently involved vessel, followed by LCX (16.67%) and LAD (5.55%). This is similar to the results of many previous studies.[13,14] However, in the Malviya study,[15] LAD involvement was the most common (59.6%), RCA accounted for 46.1%, LCX accounted for 36.5%, and LMCA accounted for 3.8%.

Similar to a previous study by Malviya et al,[4] there was no mortality in the present study. Malviya et al[4] also found that 26.9% of patients with isolated CAE had MACE events, which is higher than our study, with a result of 5.56% patients. One patient was re-hospitalized in CAE group and 2 patients for angina in control group, but no significant differences were found between the 2 groups. The pathophysiological mechanism of MI caused by isolated CAE remains unclear. Various mechanisms including slow coronary flow and altered flow dynamics have been implicated.[15,16] In the study by Gule et al,[16] Myocardial Blush Grade was used to analyze the coronary microcirculation perfusion in patients with isolated CAE and showed that angina attacks and MI in patients with isolated CAE may be related to impaired coronary microcirculation perfusion.

Risk factors for CAE are still debated. CAE has an inverse association with diabetes mellitus.[17] Several reports showed male sex is an independent risk factor for CAE.[18,19] Hypertension and smoking have been demonstrated to be associated with CAE.[20,21] In our research, the proportion of gender and smoking were similar in the 2 groups. In addition, BMI and IVSd were independent risk factors for CAE, which are similar to the previous studies.[22,23]

This study has some limitations. First, the sample of patients was relatively small and a larger study remain to be done. Another potential limitation of this study is the subjective, nonquantitative analysis of the echocardiographic images.

5. Conclusions

BMI and IVSd were independent risk factors for isolated CAE, and had a good predictive value for isolated CAE.

Author contributions

Conceptualization: Xiuchun Yang, Yijun Zong, Bing Xiao.
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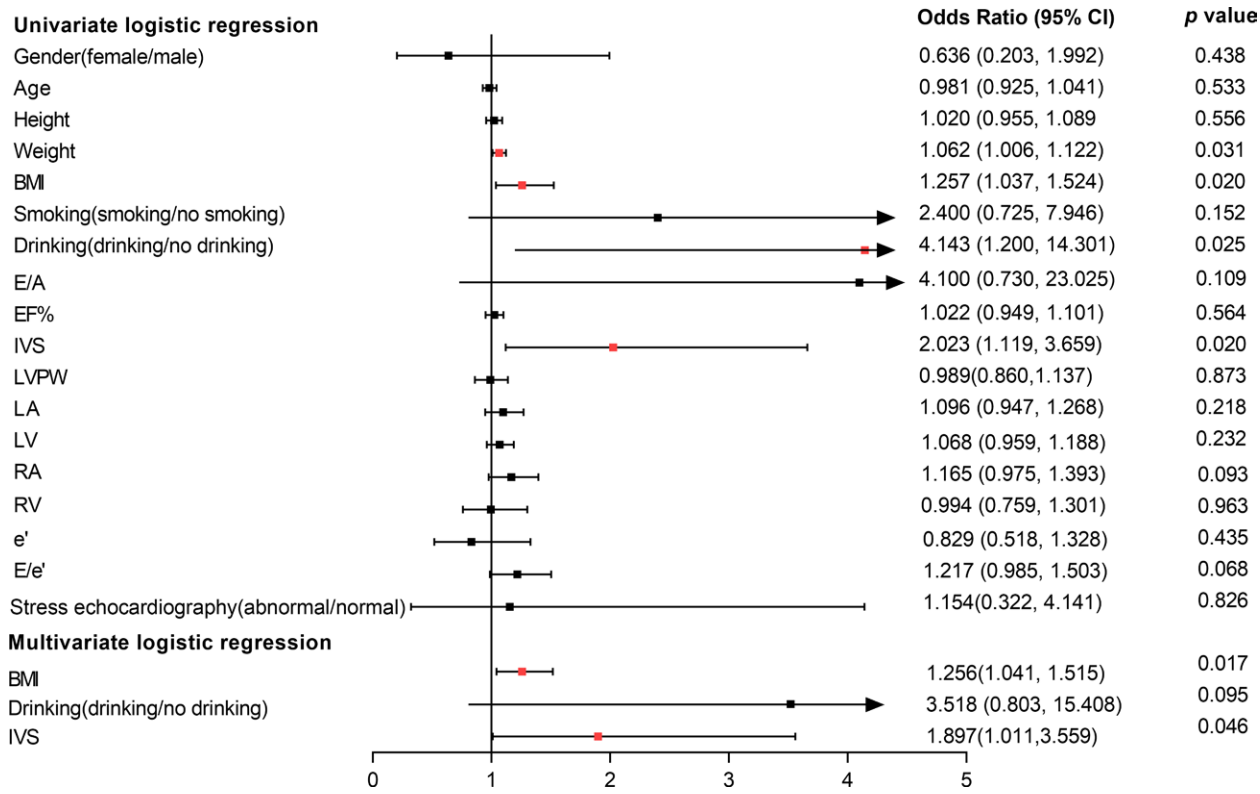

Figure 1. Multivariate logistic regression analysis results.

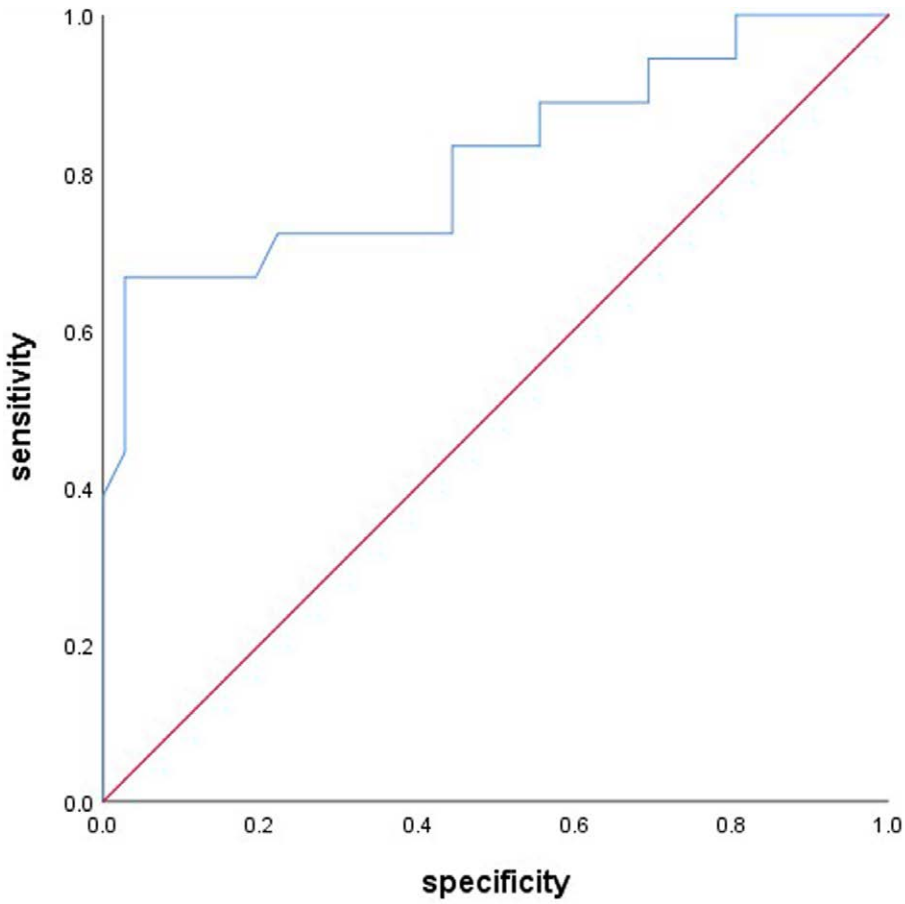

Figure 2. ROC curve. ROC = receiver operating characteristic.

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