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Cer(d18:1/16:0) as a biomarkers for acute coronary syndrome in Chinese populations

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Ceramides play a crucial role in atherosclerosis progression and have been linked to cardiovascular events. The objective of this study was to investigate the association between serum ceramide levels and Acute coronary syndrome, as well as evaluate their potential for predicting ACS in Chinese population. Data of 1327 patients with suspected or known coronary artery disease from Beijing anzhen Hospital and Handan First hospital were collected. Plasma ceramide were measured using the LC–MS/MS system. The area under the ROC curve was used to screen the most valuable predictor. Distinctive ACS-related variables were screened out using Boruta and LASSO regression. Multivariate Logistic models and restricted cubic spline analysis were conducted to examine the associations between Ceramide and ACS. Cer (d18:1/14:0), Cer (d18:1/16:0), Cer (d18:1/18:0), Cer (d18:1/20:0), Cer (d18:1/22:0), and Cer (d18:1/24:0) were significantly elevated in the ACS group. Diagnostic performance assessments showed that Cer(d18:1/16:0) had superior accuracy in detecting ACS compared to other ceramides tested. The Boruta algorithm identified 8 significant variables related to ACS. Cer(d18:1/16:0) associated with ACS were discovered using the LASSO logistic regression technique. Multivariate logistic regression models further supported the relationship between Cer(d18:1/16:0) and ACS. Additionally, a significant nonlinear relationship was observed between Cer(d18:1/16:0) and ACS, with a threshold of 150umol/L. The study found that ceramides, particularly Cer(d18:1/16:0), were significantly associated with ACS and could be a potential biomarker for predicting and diagnosing ACS in Chinese populations experiencing chest pain.

Keywords Ceramide, Acute coronary syndrome, Risk factors, Biomarkers, Lipids

Acute coronary syndrome (ACS) is a leading cause of morbidity and mortality worldwide, significantly contributing to the global burden of cardiovascular disease. Early detection and treatment of patients at risk for acute coronary events are essential for effectively mitigating this burden.

The core pathogenesis of ACS lies in the unstable state of atherosclerotic plaques and the associated pathophysiological processes[1,2]. Ceramides, known for their role in accelerating the uptake of low-density lipoprotein (LDL) particles and their penetration into the arterial wall, are involved in several key aspects of atherosclerosis progression, including inflammation and apoptosis[3]. The concentration of ceramide in these plaques is significantly higher than in the blood: histological studies have revealed that ceramide concentrations in atherosclerotic plaques are over 50 times higher than those in the blood[4]. Three ceramides—Cer(d18:1/16:0), Cer(d18:1/18:0), and Cer(d18:1/24:1)—were identified as significant predictors of sudden cardiac death and major adverse cardiovascular events (MACE)[5]. These associations have been confirmed in both secondary prevention cohorts with known CVD and primary prevention general population cohorts[6]. Therefore, as a potential biomarker, ceramide can provide valuable information for early identification, risk stratification, and treatment decision-making in patients with angina[7]. In our recent study, Cer(d18:1/16:0) was found to be significantly associated with residual inflammatory risk among CAD patients[8]. Despite many studies linking

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ceramides to cardiovascular disease severity and risk, no clinical studies have specifically investigated the diagnostic value of ceramides in ACS within the Chinese population[5,6,9].

Hence, we performed a clinical trial (Evaluating the Role of Serum Ceramide Testing in the Diagnosis of Acute Coronary Syndrome, Chinese Clinical Trial Registry) that aims to evaluate the role of seven ceramides in the adjunctive diagnosis of acute coronary syndrome. The objective of this study was to investigate the association between serum ceramide levels and ACS, as well as evaluate their potential for predicting ACS in patients who have experienced chest pain.

Methods

Study design and participants

We conducted a two Clinical Study to assess the value of plasma ceramide in the diagnosis of ACS (Chinese Clinical Trial Registry, ChiCTR-2200056697). Demographic and clinical data were collected from the departmental electronic patient information system. This study protocol was approved by the Medical Ethics Institutional Review Board at Beijing Anzhen Hospital and Handan First Hospital. The study complies with the Declaration of Helsinki. All participants provided written informed consent for participation in this study.

The recruited patients with suspected CAD were from Beijing Anzhen Hospital and Handan First Hospital, and the recruitment took place between April 2021 and May 2023. The inclusion criteria were: (1) Patients aged 18 years or older who are undergoing coronary angiography for chest pain, and (2) patients who had a complete clinical data record. The exclusion criteria were: (1) Pregnant women, (2) Patients with familial hypercholesterolemia, (3) Patients suffering from bleeding disorders, (4) Patients with neoplasms with a life expectancy < 1 year. (5) Patients with mental illness. (6) Patients with a history of drug abuse or alcohol dependence. (7) Patients with chronic kidney disease (eGFR < 60 mL/min/1.73 m^2). A total of 1327 patients were included finally.

Ceramide measurement

For laboratory analysis, blood samples taken from participants were first treated with EDTA for anticoagulation. Specifically, a volume of 500 µl of blood was collected from each individual. The plasma was swiftly separated within an hour of collection and then preserved at − 80° until the time of analysis. The ABSciex TripleQuad™ 4500MD LC–MS/MS system, manufactured by Sciex in Framingham, MA, United States, was employed for the quantification of circulating plasma ceramides. This sophisticated system facilitated the simultaneous quantification of various ceramides, including Cer(d18:1/14:0), Cer(d18:1/16:0), Cer(d18:1/18:0), Cer(d18:1/20:0), Cer(d18:1/22:0), Cer(d18:1/24:0), and Cer(d18:1/24:1). The detailed methodology for measuring ceramides has been previously published and is readily available in our recent publication[10]. Based on the measured ceramide values, we further calculated the ratios of different ceramides to Cer(d18:1/24:0), abbreviated as CerXR. For example: Cer(d18:1/14:0)R [Cer(d18:1/14:0)/Cer(d18:1/24:0)], Cer(d18:1/16:0)R [Cer(d18:1/16:0)/ Cer(d18:1/24:0)],etc.

Diagnostic protocol and data collection

Each center will form a clinical panel of four senior cardiologists to assess participants' diagnoses. The evaluation will follow guidelines from the fourth edition of the Unified Global definition of myocardial infarction, the 2017 ESC guidelines for Acute ST-segment elevation myocardial infarction, the 2015 ESC guidelines for Acute non-ST-segment elevation acute coronary syndrome, and the 2019 ESC guidelines for chronic conditions. Patients' demographic and clinical characteristics were obtained through a review of their medical records. The definition of ACS was the recording of unstable angina or acute myocardial infarction. The recorded clinical characteristics of the patients included age, sex, presence of diabetes, hypertension, and smoking status.

Statistical analysis

Sample Size: Using the PASS 15 (NCSS, LLC. Kaysville, Utah, USA), we estimated the area under the ROC curve of a diagnostic index compared to clinical diagnostic criteria to determine the required sample size. We conducted a two-sided test at a significance level (α) of 0.05 and a confidence level (1 − β) of 0.8. The AUC of the ROC curve was 0.75, with the lowest acceptable AUC set at 0.7. The ratio of patients in the clinical diagnosis negative group to the positive group was 2:5. To ensure adequate statistical power, we aimed to enroll a minimum of 741 patients with acute coronary syndrome and 296 patients without acute coronary syndrome, totaling at least 1037 participants. Accounting for a 10% dropout rate, we decided to enroll 824 patients with acute coronary syndrome and 329 patients without the syndrome. The target effective sample size for the clinical trial was set at 1200 or higher, with the acute coronary syndrome group comprising no less than 824 participants. Study endpoints: If the area under the ROC curve for any ceramide parameter reached 0.7, ceramide was considered to have an auxiliary diagnostic value for clinical acute coronary syndrome.

We started with 19 variables, including demographic characteristics, medical history and ceramide, as predictors. Continuous variables with a normal distribution, as determined by the Kolmogorov–Smirnov test, were presented as means ± standard deviation. Variables without a normal distribution were expressed as median (range). Categorical variables were presented as n (%) and analyzed using the chi-square test. Spearman's correlation test was used to assess the correlation between the ceramide variables. The differences in serum ceramide levels between the two groups (ACS group and non-ACS group) were compared using Mann–Whitney U tests. The performance of each independent ceramide in predicting ACS was determined by the area under curve (AUC). LASSO regression and the Boruta feature selection algorithm were employed to identify essential variables associated with ACS in the dataset, and distinctive ACS-related variables were screened out using these methods. Collinearity among the variables was assessed before modeling, and redundant features was removed. We employed the Boruta algorithm (maxRun = 100) by using *Boruta* package of R studio for feature selection.

Furthermore, the characteristic variables screening was based on LASSO logistic regression. For validation, univariate and multivariate logistic regression analysis were also performed to confirm the association of variables with ACS (STable 1).Then receiver operating characteristic (ROC) curve analysis was performed to assess the Cer(d18:1/16:0), and the combination of traditional risk factors in predicting ACS.

For sensitivity analysis, Cer(d18:1/16:0) was analyzed as both a continuous variable and a categorical variable to clarify its association with ACS. In Model 1, adjustment includes sex and age. In Model 2, adjustment includes sex, age, hypertension, diabete mellitus, and smoking. In Model 3, adjustment includes 12 ceramide indices. Further, restricted cubic spline regressions were fitted to investigate the potential nonlinear association between the Cer(d18:1/16:0) (continuous) and the risk of ACS. Results were reported as odds ratios (ORs) with associated 95% confidence intervals (CIs). All statistical analyses were performed in SPSS 26.0 (IBM, Inc., Chicago United States) and *R* studio with the *R version* (*R version* 4.2.2.). Statistical significance was defined as a *P*-value of less than 0.05 for a two-tailed test.

Results

Characteristics of the study population

1327 patients with suspected or known CAD were evaluated with invasive coronary angiography. Patient demographics data and ceramide parameters were summarized in Table 1. The levels of Ceramide under different groupings were demonstrated in Fig. 1. Compared with the non-ACS group, patients with ACS had higher Cer(d18:1/14:0) ($P<0.01$), Cer(d18:1/16:0) ($P<0.001$), Cer(d18:1/18:0) ($P<0.001$), Cer(d18:1/20:0) ($P<0.05$), Cer(d18:1/22:0) ($P<0.05$) and Cer(d18:1/24:0) ($P<0.05$);Cer(d18:1/24:1) ($P>0.05$) did not differ significantly between the groups.

Characteristic	Group			*P*-value
	Overall (1327)	NonACS	ACS	
Sex				<0.001
Female	444 (33.5%)	153 (46.9%)	291 (29.1%)	
Male	883 (66.5%)	173 (53.1%)	710 (70.9%)	
AGE	61 (54, 68)	62 (54, 69)	61 (54, 68)	0.405
AGE ≥ 60	737 (55.5%)	182 (55.8%)	555 (55.4%)	0.904
Hypertension	1,003 (75.6%)	240 (73.6%)	763 (76.2%)	0.342
Diabete melltius	426 (32.1%)	78 (23.9%)	348 (34.8%)	<0.001
Smoking				<0.001
Never	385 (29.0%)	135 (41.4%)	250 (25.0%)	
Former	403 (30.4%)	92 (28.2%)	311 (31.1%)	
Current	539 (40.6%)	99 (30.4%)	440 (44.0%)	
Coronary artery disease				<0.001
Non obstructive coronary artery disease	213 (16.1%)	213 (65.3%)	0 (0.0%)	
Stable coronary artery disease	113 (8.5%)	113 (34.7%)	0 (0.0%)	
Unstable angina	856 (64.5%)	0 (0.0%)	856 (85.5%)	
Acute myocardial infarction	145 (10.9%)	0 (0.0%)	145 (14.5%)	
Ceramide and ratio				
Cer(d18:1/14:0)	2.40 (1.80, 3.30)	2.30 (1.70, 3.10)	2.50 (1.80, 3.40)	0.006
Cer(d18:1/16:0)	150 (123, 183)	129 (111, 156)	157 (128, 190)	<0.001
Cer(d18:1/18:0)	41 (30, 55)	38 (28, 51)	42 (31, 56)	<0.001
Cer(d18:1/20:0)	56 (43, 72)	54 (41, 67)	57 (44, 73)	0.015
Cer(d18:1/22:0)	404 (318, 519)	391 (310, 481)	408 (320, 528)	0.024
Cer(d18:1/24:0)	1,760 (1,380, 2,230)	1,705 (1,310, 2,138)	1,790 (1,410, 2,260)	0.011
Cer(d18:1/24:1)	460 (357, 575)	448 (362, 549)	465 (352, 583)	0.188
Cer(d18:1/14:0)R	0.0014 (0.0010, 0.0019)	0.0013 (0.0010, 0.0018)	0.0014 (0.0010, 0.0019)	0.272
Cer(d18:1/16:0)R	0.085 (0.070, 0.105)	0.078 (0.064, 0.097)	0.088 (0.072, 0.107)	<0.001
Cer(d18:1/18:0)R	0.023 (0.017, 0.031)	0.022 (0.017, 0.030)	0.023 (0.017, 0.031)	0.144
Cer(d18:1/20:0)R	0.031 (0.024, 0.041)	0.031 (0.024, 0.041)	0.032 (0.024, 0.041)	0.852
Cer(d18:1/22:0)R	0.23 (0.21, 0.26)	0.23 (0.21, 0.26)	0.23 (0.21, 0.26)	0.223
Cer(d18:1/24:1)R	0.26 (0.20, 0.33)	0.26 (0.20, 0.33)	0.26 (0.20, 0.33)	0.243

Table 1. Patient demographics and baseline characteristics. n (%); Median (IQR). For categorical variables, absolute numbers (n) and relative proportions (%) are presented. For continuous variables, the median along with the interquartile range is presented.

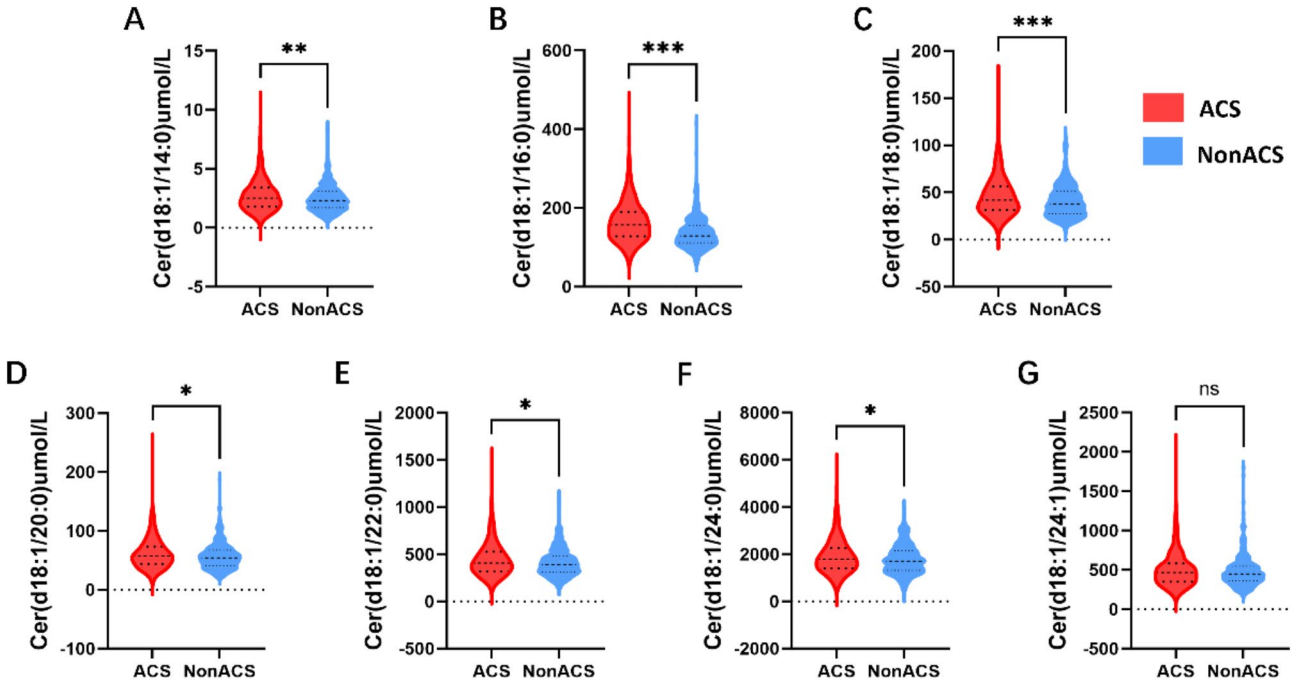

Fig. 1. Serum Ceramide levels under different groupings. Comparison of Cer(d18:1/14:0) (**A**), Cer(d18:1/16:0) (**B**), Cer(d18:1/18:0) (**C**), Cer(d18:1/20:0) (**D**), Cer(d18:1/22:0) (**E**), (d18:1/24:0) (**F**), Cer(d18:1/24:1) (**G**) between ACS patients and non-ACS patients.

Variables selection

Spearman test was conducted to assess the correlation between ceramides, revealing a significant positive correlation among them, as depicted in the Fig. 2. The results of the correlation analysis indicated a high degree of collinearity among the independent variables (STable 2). Cer(d18:1/22:0) was excluded due to its higher VIF value, and collinearity among the remaining variables was assessed again (STable 3). The Boruta algorithm identified eight significant variables related to ACS (STable 4). Four ceramides (Cer(d18:1/16:0), Cer(d18:1/18:0), Cer(d18:1/24:0), and Cer(d18:1/24:1)) were chosen as potential variables based on previous studies. Finally, Cer(d18:1/16:0) associated with ACS was discovered using the LASSO logistic regression technique (Fig. 3).

Diagnostic performance of ceramides for ACS

The diagnostic performance of Cer(d18:1/16:0)(cut-off value 150umol/L) for detecting ACS, measured by sensitivity, accuracy, PPV and AUC, was significantly better than those of Ceramide(Table 2). Moreover, Cer(d18:1/20:0) had the highest specificity (83.1%), but lower sensitivity(25.6%) and NPV(26.6%). ROC curve analysis was performed to evaluate the performance of Ceramide in predicting ACS (Fig. 4A). As shown in Fig. 4B. the AUC of ROC curve for traditional risk factors such as Hypertension, Diabete, and Smoking in predicting severe ACS alone were 0.513 (95% CI 0.486–0.540), 0.554 (95% CI 0.527–0.582), and 0.597 (95% CI 0.563–0.540). And the AUC can increase to 0.678 (95% CI 0.646–0.711) and 0.683 (95% CI 0.650–0.715) by combining the Cer(d18:1/16:0). Furthermore, the Smoking combining Cer(d18:1/16:0) showed further improved ability in predicting ACS (AUC = 0.702, 95% CI 0.670–0.734).

Association between Cer(d18:1/16:0) and ACS

As indicated in Table 3, three different models (logistic regression models) were constructed to evaluate the correlation between Cer(d18:1/16:0) and ACS. Adjustment was made for demographic variables in Model 1 and Model 2, while different ceramide indicators were considered in Model 3. Despite these adjustments, Cer(d18:1/16:0) maintained a positive correlation with ACS. This correlation persisted even when Cer(d18:1/16:0) was converted into a categorical variable.

The nonlinearity is addressed by the logistic regression model with a restricted cubic spline

The RCS analysis revealed a non-linear association between Cer(d18:1/16:0) and ACS, with an inflection point detected at Cer(d18:1/16:0) = 150 umol/L (Fig. 5). Using the inflection point, the data was stratified into two groups, and segmented regression was then performed on each group separately: Cer(d18:1/16:0) < 150 umol/L [OR (per 1SD) = 1.29, 95% CI 1.10–1.51, $P = 0.002$] and Cer(d18:1/16:0) ≥ 150 umol/L [OR (per 1SD) = 1.46, 95% CI 1.11–1.93, $P = 0.007$] (STable 5).

Fig. 2. Spearman correlation analysis of correlation between ceramides. The color of the square shape represent the value of the correlation coefficient. The darker the color of the square, the larger the absolute value of the correlation coefficient; the color of the square corresponds to the value of the correlation coefficient on the color scale. The main diagonal of a correlation matrix represents the correlation of each variable with itself, which is shown in gray and described as corresponding to a coefficient of 1.*$P<0.05$, **$P<0.01$, ***$P<0.001$.

Discussion

The findings of this study demonstrate that Cer(d18:1/16:0) is an independent biomarker significantly associated with ACS. Moreover, a nonlinear relationship with a positive correlation between Cer(d18:1/16:0) and ACS was observed using RCS models. The first study, to the best of our knowledge, also presented alternative cut-off points for Cer(d18:1/16:0) levels for diagnosing ACS in the Chinese population. This is conducive to optimizing clinical management strategies.

Some previous studies have shown consistent results with ours investigating the correlation between Cer(d18:1/16:0) and ACS. Previous clinical research found that elevated ceramide plasma concentrations are associated with coronary plaque vulnerability evaluated by endovascular imaging[11,12]. Laaksonen found higher expression levels of certain ceramides in ACS patients compared to stable coronary heart disease patients[13]. Advances in lipidomics have identified circulating ceramides as significant predictors of atherosclerotic cardiovascular events[14]. In comparison to traditional cardiovascular disease risk factors, ceramide—a bioactive sphingolipid—has demonstrated enhanced predictive abilities for cardiovascular disease events[15]. Ceramide risk scores, derived from high-risk ceramide subtypes (Cer(d18:1/16:0), Cer(d18:1/18:0), Cer(d18:1/24:1)) identified in previous studies, have been developed and adapted for routine clinical practice[6,16]. Research in rodents shows that ceramides contribute to cardiovascular diseases by causing metabolic issues. Interventions that either reduce

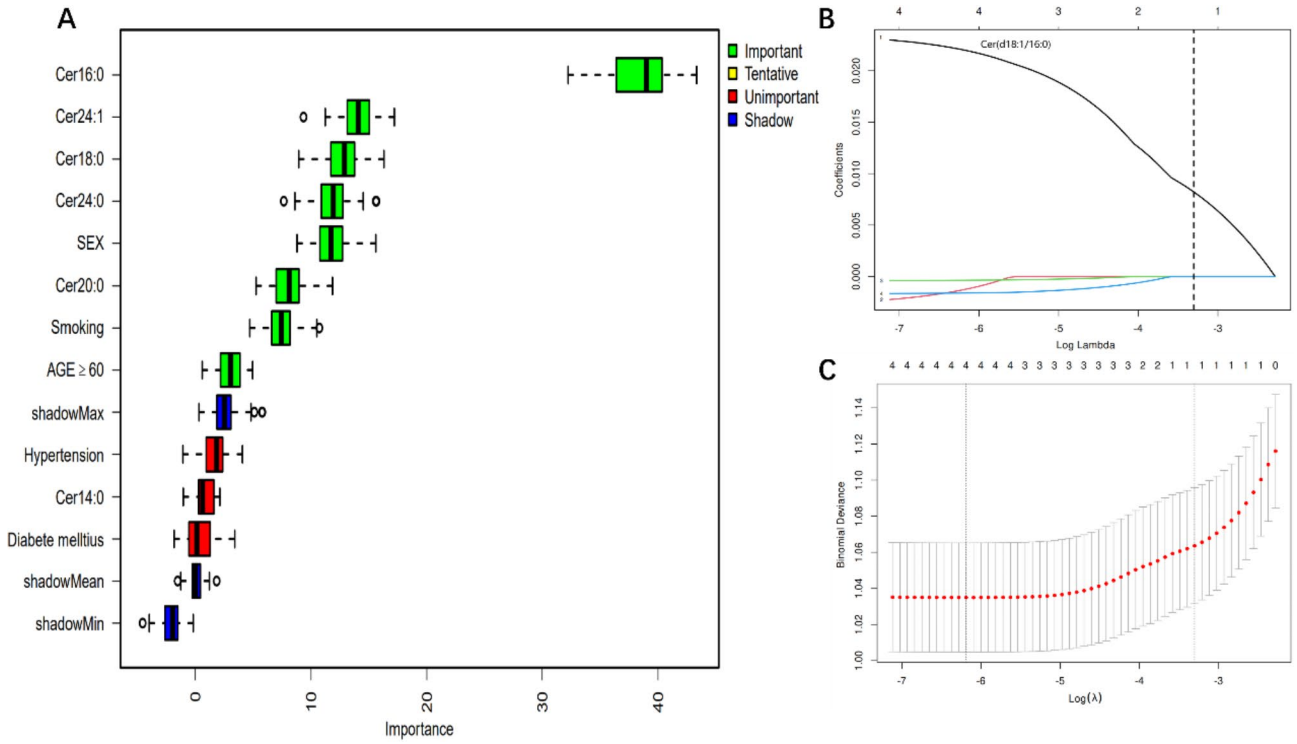

Fig. 3. Screening of characteristic variable-related diagnositic signature in ACS using Lasso.cv and Boruta. (**A**) Relevant features (highlighted in green) to the interest selected with Boruta algorithm. (**B**) Lasso regression and tenfold cross-validation were used to select the ceramide features. LASSO coefficient profile are plotted against the log (λ) sequence. (**C**) Partial likelihood deviance for different numbers of variables, there are 1 non-zero coefficients (Cer(d18:1/16:0)) obtained according to the λ value.

	AUC	Accuracy (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Cer(d18:1/14:0)	0.551 (0.516–0.586)	48.9	44.0	66.6	80.1	27.8
Cer(d18:1/16:0)	0.678 (0.645–0.710)	61.3	58.7	69.3	85.4	35.3
Cer(d18:1/18:0)	0.565 (0.530–0.600)	46.5	38.4	71.5	80.5	27.4
Cer(d18:1/20:0)	0.545 (0.509–0.580)	39.7	25.6	83.1	82.3	26.6
Cer(d18:1/22:0)	0.542 (0.506–0.577)	44.5	32.8	75.5	80.3	26.7
Cer(d18:1/24:0)	0.547 (0.512–0.583)	51.8	49.3	59.8	79.0	27.7
Cer(d18:1/24:1)	0.524 (0.489–0.559)	51.4	49.3	58.0	78.2	27.1

Table 2. Diagnosis accuracy assessment of ceramides in predicting ACS. Data are expressed as n (95% confidence interval).

ceramide production or increase their breakdown improve conditions like atherosclerosis, insulin resistance, fatty liver disease, and cardiomyopathy[17,18]. Study in mouse models shows that ASM and ceramide signaling critically mediate hypocholesterolemia-induced NLRP3 inflammasome activation in endothelial cells, leading to endothelial dysfunction, vascular inflammation, and atherosclerosis[19]. Hammerschmidt et al. revealed that the CerS6/Cer16:0/Mff(mitochondrial fission factor) pathway regulates mitochondrial dynamics and insulin resistance in obesity, proposing the interaction between CerS6-derived sphingolipids and Mff as a therapeutic target for metabolic diseases[20]. They represent a promising class of molecules with considerable therapeutic potential and clinical applicability.

Proinflammatory effects mediated by ceramide signaling increase plaque vulnerability[21]. Our study shows that Cer(d18:1/16:0) is independently linked to ACS, which can partially explain the results. Possible underlying mechanisms by which specific plasma ceramides might contribute to the pathophysiology of atherosclerosis are not fully understood. Schissel et al. found that the physiological process of ceramide-mediated deposition of LDL-C into the vessel wall can aggravate the instability of atherosclerotic plaques, making them more prone to rupture [22]. Moreover, ceramide levels (Cer16:0) were elevated in arterial lipid plaques, which caused human coronary artery smooth muscle cell (HCASMC) apoptosis/necrosis, leading to a thinner fibrous cap and an increased risk of plaque rupture[23,24]. Previous data indicate that various ceramides may increase in cases of pulmonary arterial hypertension, type 2 diabetes, and insulin resistance[25–27]. This study also applied RCS models

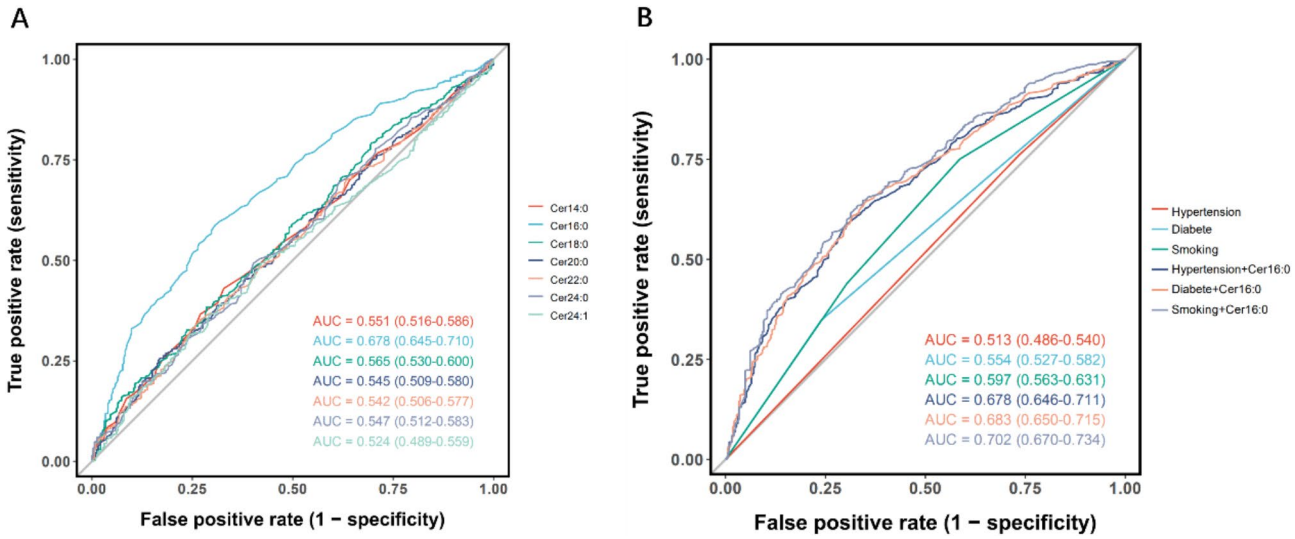

Fig. 4. ROC curves of Ceramide and their combination showing different abilities to predict ACS.

Characteristic	Model 1		Model 2		Model 3	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Cer(d18:1/16:0) as a continuous variable						
Cer(d18:1/16:0)	1.02 (1.01, 1.02)	< 0.001	1.01 (1.01, 1.02)	< 0.001	1.03 (1.01, 1.04)	< 0.001
Cer(d18:1/16:0) (per 1SD)	2.15 (1.73, 2.45)	< 0.001	2.13 (1.79, 2.53)	< 0.001	3.01 (1.62, 5.58)	< 0.001
Cer(d18:1/16:0) as a categories variable (Quartiles)						
Cer(d18:1/16:0)						
Q1	Reference					
Q2	1.62 (1.16, 2.26)	0.005	1.62 (1.21, 2.36)	0.002	1.69 (1.14, 2.50)	< 0.001
Q3	2.74 (1.91, 3.92)	< 0.001	2.84 (1.98, 4.07)	< 0.001	2.97 (1.72, 5.11)	< 0.001
Q4	6.61 (4.23, 10.32)	< 0.001	7.18 (4.62, 11.16)	< 0.001	7.38 (3.02, 18.00)	< 0.001
P for trend		< 0.001		< 0.001		< 0.001

Table 3. Association between Cer(d18:1/16:0) and ACS. OR = Odds Ratio, CI = Confidence Interval. Model 1: adjusted for Male, Age; Model 2: adjusted for Male, Age, Hypertension, Diabete, Smoking; Model 3: adjusted for 12 Ceramide indices (Cer(d18:1/14:0), Cer(d18:1/18:0), Cer(d18:1/20:0), Cer(d18:1/22:0), Cer(d18:1/24:0), Cer(d18:1/24:1), Cer(d18:1/14:0)R, Cer(d18:1/16:0)R Cer(d18:1/18:0)R, Cer(d18:1/20:0)R, Cer(d18:1/22:0)R, Cer(d18:1/24:1)R).

to assess a nonlinear relationship, allowing for an in-depth analysis of the correlations between Cer(d18:1/16:0) and ACS. Combined with previous research, we believe that Cer(d18:1/16:0) may play a significant role in the pathophysiology of coronary atheroma plaque rupture and could potentially serve as a novel biomarker for ACS.

Strength and limitation

Our study possesses inherent strengths which are listed below. Firstly, to mitigate the inherent limitations of a cross-sectional study design, we substantially enlarged our study population and employed machine learning techniques to identify key variables. Secondly, we verified the strength of the results through sensitivity analysis, which involved transforming variable forms, such as normalization or reclassification, and conducting subgroup analyses. Lastly, our study was the first to focus on the Chinese population to determine the relationship between ceramide and ACS, ours study highlights a nonlinear relationship and identifies an inflection point in the correlation between ceramide levels and ACS. However, it had to be acknowledged that there were some limitations. First of all, we did not examine the causal relationship between ceramide and ACS due to the cross-sectional study design in this paper. Second, our study focused solely on ceramides and did not take into account other clinical markers, such as cholesterol et.al. In addition, fewer patients with acute myocardial infarction were included in the study population. Additional studies are required to investigate the diagnostic and prognostic value of ceramides in ACS by conducting follow-up assessments in various clinical models among diverse populations. Additionally, it is important to note that female patients in our study were predominantly postmenopausal; therefore, the results' external generalizability should not make a substantial difference.

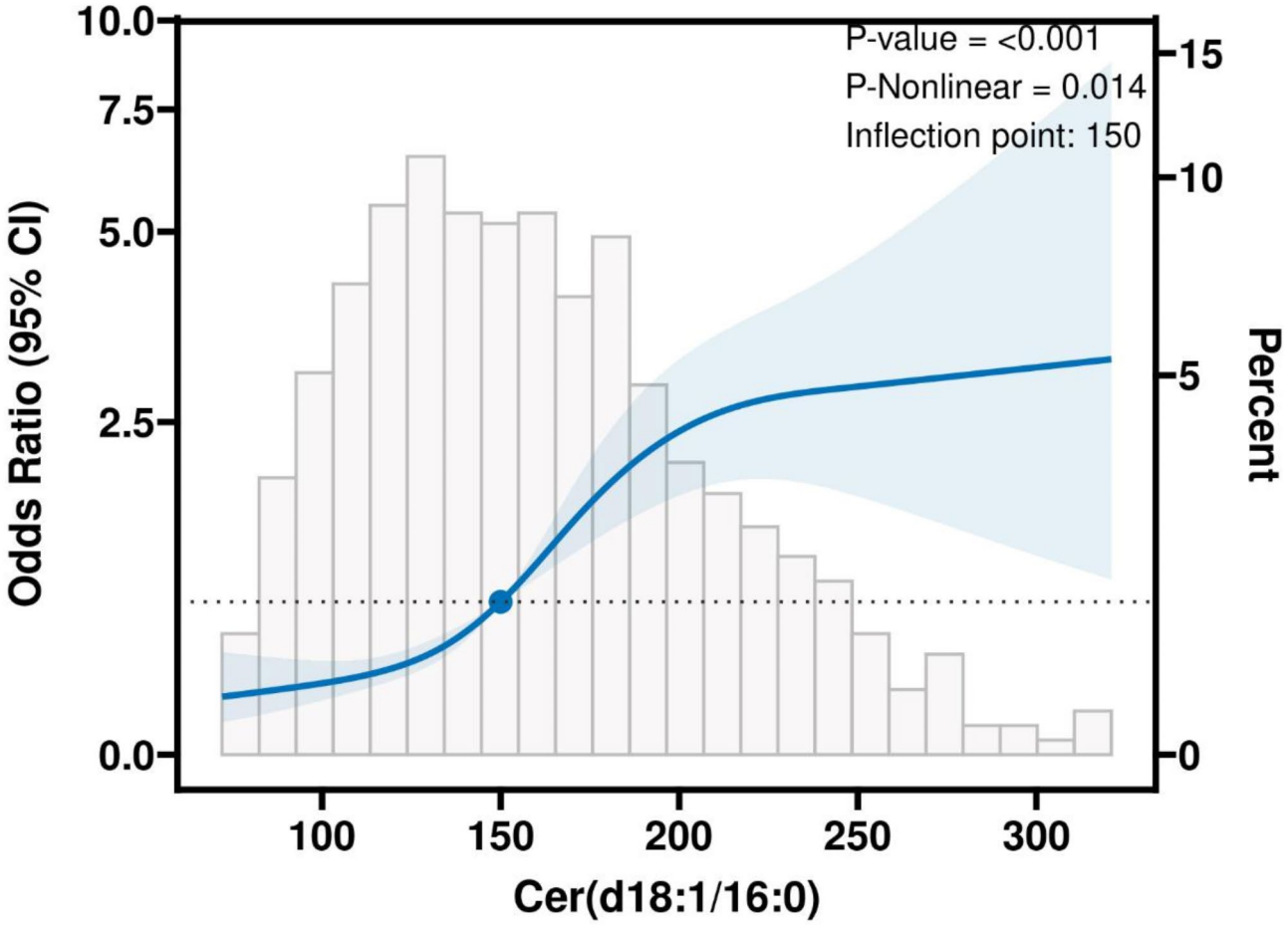

Fig. 5. Nonlinear relationship between Cer(d18:1/16:0) and ACS. Adjustment for age, male, hypertension, diabetes mellitus, and smoking. The solid lines represent OR, and blue areas indicate the 95% CIs.

Conclusion

Our study demonstrated a positive association between Ceramide and ACS, especially Cer(d18:1/16:0). The combination of Cer(d18:1/16:0) and traditional risk factors may help identify ACS patients from those with suspected CAD.

Data availability

All data generated or analysed during this study are included in this published article.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

This study complied with the Declaration of Helsinki and received approval from the Ethics Committee of Beijing Anzhen Hospital, affiliated with Capital Medical University.

Consent for publication

All authors have reviewed and approved the final version of the manuscript. All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers.

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