A New Potential Predictor of Coronary Artery Disease: The Ratio of Mitral Peak Filling Velocity to Mitral Annular Velocity in Early Diastole

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

CDE Li Ma
B   Yanhong Li
B   Zhisheng Wu
AFG Yuming Mu

Department of Echocardiography, First Affiliated Hospital, Xinjiang Medical University, Urumqi, Xinjiang, P.R. China

Corresponding Author: Yuming Mu, e-mail: mym1234@126.com
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Background: The aim of this study was to explore the value of the ratio of mitral peak filling velocity (E) to mitral annular velocity (e') in early diastole as a predictor of coronary artery disease (CAD).

Material/Methods: The study population consisted of 83 consecutive patients (aged 38–77 years, 22 women and 61 men) who received coronary angiography. The E/e' ratio was estimated by echocardiographic examination. Statistical significance was determined by receiver operating characteristic (ROC) curve and multiple logistic regression analyses.

Results: ROC curve analysis showed that the optimal E/e' ratio cut-off for predicting CAD was 8.153 with a specificity of 72.4% and sensitivity of 57.4%. The area under the ROC curve was 0.635 with a 95% confidence interval (CI) for normal distribution of 0.515–0.755 (p=0.043). Multivariate logistic regression analysis demonstrated that the E/e' ratio was closely associated with CAD (odds ratio [OR], 1.350; 95% CI, 1.087–1.676, p=0.007).

Conclusions: The E/e' ratio is a simple and practical predictor of CAD and may be an independent risk factor for CAD. Large-cohort and multi-center studies are required to confirm these observations.

MeSH Keywords: Atrial Function, Left • Coronary Disease • Heart Failure, Diastolic

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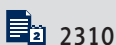
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Background

Diastolic dysfunction has been shown to be valuable in predicting the development of evident heart failure and all-cause mortality [1–3]. Echocardiography, as a non-invasive technique, is the most common technique clinically employed for evaluating left ventricular (LV) diastolic function. In routine echocardiographic examination, tissue Doppler imaging (TDI) can provide measurements of the early mitral filling peak velocity of blood flow (E) and early diastolic mitral annular velocity (e'), and the ratio of these measurements (E/e') is widely regarded to be a non-invasive substitute for LV diastolic function [4–7]. The early diastolic e' determined by TDI can be used to represent LV myocardial relaxation, and the E/e' ratio, together with the mitral peak early filling velocity E, is recommended for determination of the LV diastolic function by the ASE and the European Society of Cardiology (ESC) [8,9].

An E/e' ratio <8 is normal, and a value >15 indicates the presence of diastolic dysfunction, in which E is faster due to elevated filling pressures and e' is slower due to increased left ventricular stiffness. Diastolic dysfunction generally occurs prior to systolic dysfunction in coronary artery disease (CAD) [10,11], and the early determination of diastolic dysfunction in advance of the emergency of LV ejection fraction (LVEF) decline might facilitate the prediction of CAD. Although a study previously reported that LV diastolic abnormalities evaluated by Doppler echocardiography can predict myocardial infarction-linked mortality and morbidity [12], and known or suspected CAD with preserved EF [13,14], the diagnostic accuracy of non-invasively determined diastolic function has not been well investigated. Specifically, whether the E/e' ratio determined by TDI can be used to predict CAD has remained unclear. We hypothesized that the E/e' ratio is closely associated with CAD and can be used as a predictor of CAD. Therefore, we examined the predictive value of the E/e' ratio for CAD in patients undergoing routine echocardiography.

Material and Methods

The study protocol conformed to the ethics principles regarding human experimentation of the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University, Xinjiang Uygur Autonomous Regions, China. The study was carried out in compliance with the approved guidelines.

Patients

Eighty-three consecutive adult patients (61 men and 22 women, age 38–77 years), who had already been diagnosed with coronary atherosclerosis or were suspected of CAD by coronary angiography in the First Affiliated Hospital of Xinjiang Medical University in China, were recruited from December 20, 2013 to July 31, 2014 for this study. Conventional two-dimensional (2D) and three-dimensional (3D) echocardiographic examinations were carried out for all participants. The inclusion criteria were: 1) typical angina and atypical chest pain; and 2) abnormal finding in an ECG with ST-T changes. Patients who had 1 or more of the following were excluded from our study: 1) spastic angina pectoris; 2) cardiac failure; 3) recent infection within 2 weeks; 4) adrenal or thyroid abnormality; 5) cardiomyopathy, valvular heart disease, or congenital heart disease; and 6) arrhythmia such as atrial fibrillation, atrial flutter, or frequent ventricular ectopy.

Clinical measurements and data collection

Blood pressure readings were taken routinely using hematomanometer at the participants' arms. Average blood pressure values were obtained from 3 independent readings. Fasting blood glucose (FBG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), and triglycerides (TG) levels were detected using a chemical analyzer (Roche Diagnostics, COBAS 8000).

A standardized questionnaire was used to assess the status of cigarette and alcohol use. No smoking in the past and at present was recorded as "never smoking". A smoking status that included both past and present smoking was recorded as "smoking". Alcohol intake was categorized as "never drinking" and "drinking", the latter of which included both past and present drinking of more than 50 g/week of alcohol [15].

Coronary angiography

Angiography was used to evaluate coronary artery stenosis and diagnose CAD. Briefly, coronary angiography was carried out using a radial approach with 6F catheters (30 frames/s) with the injection of isosorbide dinitrate (ISDN; 2.5 mg/5 ml solution injected over 20 s), according to the Judkins technique [16]. Independent investigators visually assessed the luminal narrowing in multiple segments on coronary angiograms as recommended by the American Heart Association/American College of Cardiology classification of the coronary tree. Significant CAD was defined as >50% stenosis in at least 1 major epicardial coronary artery, and controls were determined by <50% stenosis of all the major epicardial coronary arteries [17]. Classification of coronary atherosclerosis was performed according to the Gensini scoring system based on the degree of coronary artery luminal narrowing and the corresponding geographic significance. Briefly, a Gensini score of 1 represented a decrease in the lumen diameter by 25% with the roentgenographic appearance of atherosclerotic plaques. Accordingly, Gensini scores of 2, 4, 8, 16, and 32 represented

decreases in the lumen diameter by 50%, 75%, 90%, 99%, and complete occlusion, respectively. The primary vascular parts were given the following multipliers according to the myocardial region functional importance as previously described [18]: 1) ×5 for the left main coronary artery; 2) ×2.5 for the proximal segments of both the circumflex artery and the left anterior descending coronary artery (LAD); 3) ×1.5 for the mid-segment of the LAD; 4) ×1 for the obtuse marginal artery, the posterolateral artery, the distal segment of the LAD, and the right coronary artery; and 5) ×0.5 for the others.

Echocardiography

According to the guidelines of the American Society of Echocardiography (ASE), participants underwent cardiac echocardiographic examination including 2D spectral Doppler, color Doppler flow, and TDI separately [19,20] using a Vivid E9 instrument (GE Medical Systems, Horten, Norway). Echocardiograms were digitally documented and analyzed using the digital analysis system (Echo PAC BT112 software, GE Vingmed Ultrasound AS).

The LV end-diastolic diameter (LVDd) and LV end-systolic diameter (LVDs) were measured using M-mode echocardiography. The LV end-diastolic volume (EDV) and LV end-systolic volume (ESV) were calculated automatically through an adjusted Simpson's method from the apical 2-chamber and 4-chamber views, respectively. The LVEF was calculated using the following equation: EF=(EDV–ESV)/EDV×100%. The transmitral flow velocity was recorded from the sample volume at the mitral leaflet tips. The early diastolic filling peak velocity (E) and atria filling peak velocity (A) were recorded, and the ratio of E to A (E/A) was computed. Myocardial tissue velocities at different sites of the mitral annulus were determined by TDI at the long-axis from the 4-chamber view. The early diastolic mitral annular velocity (e') and late diastole (a') were measured, and average values were obtained from 5 incessant beats. The E/e' ratio was also computed [21].

Statistical analyses

The Statistics Package for Social Sciences (ver. 16.0; SPSS Inc., Chicago, IL, USA) was used to analyze the significance of the data. Four groups of patients were established based on quartile readings of the E/e' ratio as the cut-off points. Hence, each group had a similar sample size to minimize the potential sample collection bias. Normally distributed data including systolic blood pressure (SBP), diastolic blood pressure (DBP), age, TC, HDL-c, LDL-c, TG, LVDd, LVEF, E, A, e', a', and E/e' are expressed as mean ± standard deviation (SD) and were compared among groups by 1-way analysis of variance (ANOVA) followed by independent-samples t tests. The skewed FBG, E/A, LVDs, and Gensini score data are presented as median (quartile range)

and were compared using the Kruskal-Wallis test and Mann-Whitney U Test. Differences in categorical variables, including drinking status, smoking status, and sex, were analyzed by the chi-square test. The Pearson and Spearman 2-way correlation test was employed to evaluate correlations between 2 quantitative variables. Receiver operator curve (ROC) analysis was also conducted to evaluate the ability of the E/e' ratio and other traditional risk factors for predicting CAD [22], and univariate and multiple logistic regression analyses were used to identify independent predictors of E/e'. A p value <0.05 indicated significance.

Results

Comparison of basic clinical characteristics between groups

The demographic, clinical, and echocardiographic characteristics of the patients in each group are shown in Table 1. Significant differences were observed between the CAD and control groups in terms of sex (p=0.024), HDL-c (p=0.045), LVDd (p=0.030), e' (p=0.033), and E/e' (p=0.031), although the average E/e' in CAD subjects was higher than that in control participants (9.218±3.098 vs. 7.895±2.298; Figure 1).

Comparison of basic clinical and echocardiographic characteristics between groups divided by E/e' quartiles

The E/e' values of the study participants ranged from 4.17 to 18.25 with a median value of 8.00 (quartile range, 6.67–10.63). The demographic, clinical, and echocardiographic characteristics of the participants in groups based on the quartile values of the E/e' ratio are shown in Table 2. The results indicated significant differences in the distributions of age (p=0.013), HDL-c (p=0.040), LVDd (p=0.039), E (p=0.000), A (p=0.016), E/A (p=0.035), and e' (p=0.000) between the groups, and the incidence of CAD (p=0.036) differed significantly between the groups.
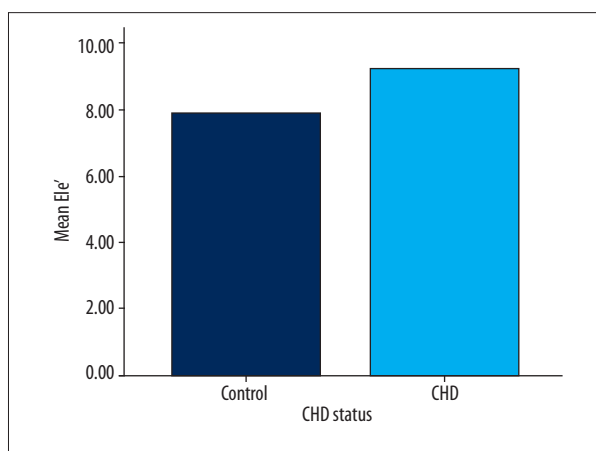
Pearson or Spearman correlations between E/e' and other demographic, clinical, and echocardiographic characteristics

The Pearson or Spearman correlation analysis results for associations between E/e' and other demographic, clinical, and echocardiographic characteristics are presented in Table 3. The analysis showed that E/e' was positively associated with age (r=0.350, p=0.001), SBP (r=0.269, p=0.014), TC (r=0.231, p=0.035), TG (r=0.217, p=0.049), FBG (r=0.300, p=0.006), E (r=0.440, p=0.000), and A (r=0.310, p=0.004) (Figure 2), and E/e' was inversely associated with e' (r=−0.742, p=0.000).

Table 1. The characteristics of the subjects with and without CHD.

Characteristic	With CHD (n=54)	Without CHD (n=29)	T or Z or chi-square test	P
Age (years)	57.83±10.35	57.72±12.77	−0.042	0.966
Sex (male/female)	44/10	17/12	5.062	0.024
Smoking status (yes/no)	27/27	10/19	1.839	0.175
Drinking status (yes/no)	14/40	8/21	0.027	0.870
Total cholesterol (mmol/L)	3.97±1.18	4.29±0.97	1.296	0.199
Triglycerides (mmol/L)	1.92±1.16	1.64±0.96	−1.123	0.265
Glucose (mmol/L)	5.19 (4.76~6.33)	5.11 (4.55~6.00)	−0.778	0.436
HDL-C (mmol/L)	1.01±0.28	1.14±0.29	2.041	0.045
LDL-C (mmol/L)	2.37±0.89	2.65±0.84	1.397	0.168
SBP (mmHg)	154±33	143±31	−1.412	0.162
DBP (mmHg)	96±23	88±21	−1.515	0.134
LVDd (mm)	49.50±4.11	47.59±2.98	−2.213	0.030
LVDs (mm)	32 (30–35)	30 (29–33)	−1.890	0.059
LVEF (%)	62.54±4.99	63.97±3.37	1.379	0.172
E (cm/s)	0.73±0.16	0.73±0.14	−0.075	0.940
A (cm/s)	0.86±0.18	0.78±0.22	−1.738	0.086
E/A	0.80 (0.70–1.13)	0.83 (0.71–1.35)	−1.657	0.097
e' (cm/s)	0.09±0.02	0.10±0.02	2.166	0.033
a' (cm/s]	0.10±0.02	0.11±0.03	1.150	0.254
E/e'	7.895±2.298	9.218±3.098	−2.206	0.031

CHD – coronary heart disease; HDL-c – fasting high-density lipoprotein cholesterol; LDL-c – fasting low-density lipoprotein cholesterol; SBP – systolic blood pressure; BP – diastolic blood pressure; LVDd – LV end-diastolic diameter; LVDs – LV end-systolic diameter; LVEF – the LV ejection fraction, the peak velocity of early rapid filling; A – atrial filling velocity; E/A – E wave/A wave ratio; e' – the peak velocities during early diastole; a' – the peak velocities during late diastole; E/e' – mitral flow E wave velocity/lateral annular e' wave velocity by TDI.

Figure 1. Level distribution of *E/e'* between the CHD and control subjects (the bar represents the mean of *E/e'*).

ROC curve analysis of the predictive value of *E/e'* for CAD

To further explore the applicability of *E/e'* relative to classical risk factors as a potential diagnostic biomarker of CAD, ROC analyses were performed, and the results are shown in Table 4. The area under the ROC (AUC) values were 0.635 for *E/e'* (95% confidence interval [CI]: 0.515–0.755, *p*=0.043; Figure 2), 0.651 for HDL-c (95% CI: 0.527–0.775, *p*=0.024; Figure 3), 0.645 for LVDd (95% CI: 0.524–0.765, *p*=0.031; Figure 4), and 0.643 for *e'* (95% CI: 0.519–0.767, *p*=0.032; Figure 5). The optimal cut-off

Table 2. Age and clinical and biochemical characteristics in patients grouped according to *E/e'* using quartile values as cut-off points.

Variable	E/e'				F or chi-square test	P
	0–6.67 (n=21)	6.68–8.00 (n=21)	8.01–10.63 (n=21)	≥10.64 (n=20)		
Age (years)	54.71±11.761	54.29±9.062	58.24±11.593	64.25±9.883	3.810	0.013
Sex (M/F)	18/3	13/8	16/5	14/6	3.261	0.353
Smoking (yes *vs.* no)	9/12	10/11	9/12	9/11	0.130	0.988
Drinking (yes *vs.* no)	6/15	4/17	7/14	5/15	1.171	0.760
Total cholesterol (mmol/L)	3.606±1.175	4.196±1.035	4.139±0.853	4.410±1.283	2.014	0.119
Triglycerides (mmol/L)	1.341±0.611	1.971±1.118	1.783±0.741	2.208±1.566	2.434	0.071
Glucose (mmol/L)	5.110 (4.575–6.555)	5.180 (4.615–6.000)	5.160 (4.650–6.020)	5.100 (4.785–7.608)	0.879	0.830
HDL-C (mmol/L)	1.134±0.355	1.026±0.213	0.919±0.167	1.136±0.330	2.892	0.040
LDL-C (mmol/L)	2.154±0.923	2.577±0.911	2.540±0.606	2.608±0.997	1.237	0.302
SBP (mmHg)	142.10±32.807	144.95±34.442	151.43±28.398	163.05±32.766	1.704	0.173
DBP (mmHg)	91.57±27.522	93.76±25.068	92.90±18.695	94.05±16.198	0.051	0.985
Gensini score	7.000 (0.000–67.500)	0.0.00 (0.000–12.250)	25.000 (0.000–63.500)	12.500 (3.250–36.500)	6.975	0.073
CHD (yes *vs.* no)	13/8	9/12	15/6	17/3	8.519	0.036
LVDd (mm)	49.43±3.641	46.76±2.998	49.67±3.851	49.50±4.286	2.922	0.039
LVDs (mm)	32.00 (30.00–34.00)	30.00 (28.00–33.00)	32.00 (30.50–34.00)	32.00 (29.25–34.75)	6.931	0.074
LVEF (%)	62.76±4.061	64.10±2.755	62.81±5.802	62.45±5.083	0.529	0.663
E (cm/s)	0.625±0.116	0.751±0.124	0.742±0.151	0.815±0.153	6.895	0.000
A (cm/s]	0.812±0.220	0.738±0.155	0.851±0.184	0.929±0.187	3.649	0.016
E/A	0.756 (0.692–0.857)	1.058 (0.799–1.360)	0.814 (0.665–1.227)	0.860 (0.698–1.166)	8.602	0.035
e' (cm/s)	0.111±0.020	0.101±0.016	0.081±0.017	0.065±0.014	30.393	0.000
a' (cm/s)	0.110±0.029	0.103±0.023	0.098±0.022	0.095±0.019	1.652	0.184

CHD – coronary heart disease; HDL-c – fasting high-density lipoprotein cholesterol; LDL-c – fasting low-density lipoprotein cholesterol; SBP – systolic blood pressure; BP – diastolic blood pressure; LVDd – LV end-diastolic diameter; LVDs – LV end-systolic diameter; LVEF – the LV ejection fraction, the peak velocity of early rapid filling; *A* – atrial filling velocity; *E/A* – E wave/A wave ratio; *e'* – the peak velocities during early diastole; *a'* – the peak velocities during late diastole; *E/e'* – mitral flow E wave velocity/lateral annular *e'* wave velocity by TDI.

point, sensitivity, specificity, and Youden index for each of these variables are listed in Table 5.

Identification of potential risk factors for CAD by univariate logistic regression analysis

The potential for variables compared between the CAD and control groups to serve as risk factors for CAD was assessed by univariate logistic regression analysis (Table 6). The risk for CAD among female participants was 67.8% less (OR, 0.322; 95% CI, 0.117–0.883, *p*=0.028) that that among male participants. In addition, the risk for CAD increased with increasing values of LVDd (OR, 1.157; 95% CI, 1.011–1.323, p=0.034) and with decreasing values of e' (OR, 0.000; 95% CI, 0.000–0.312, *p*=0.038).

Table 3. Pearson or Spearman correlations between *E/e'* and age and clinical and biochemical characteristics.

Variable	E/e'	
	Correlation coefficient	P value
Age (years)	0.350	0.001
Systolic blood pressure (mmHg)	0.269	0.014
Diastolic blood pressure (mmHg)	0.105	0.343
Cholesterol (mmol/L)	0.231	0.035
Triglycerides (mmol/L)	0.217	0.049
Glucose (mmol/L)	0.300	0.006
HDL-C (mmol/L)	0.054	0.629
LDL-C (mmol/L)	0.164	0.139
LVDd (mm)	0.075	0.503
LVDs (mm)	0.043	0.701
LVEF (%)	0.003	0.982
E (cm/s)	0.440	0.000
A (cm/s]	0.310	0.004
E/A	0.059	0.598
e'	−0.742	0.000
a'	−0.186	0.092
Gensini	0.184	0.096

HDL-c – fasting high-density lipoprotein cholesterol; LDL-c – fasting low-density lipoprotein cholesterol; LVDd – LV end-diastolic diameter; LVDs – LV end-systolic diameter; LVEF – the LV ejection fraction, the peak velocity of early rapid filling; *A* – atrial filling velocity; *E/A* – E wave/A wave ratio; *e'* – the peak velocities during early diastole; *a'* – the peak velocities during late diastole; *E/e'* – mitral flow *E* wave velocity/lateral annular *e'* wave velocity by TDI.

Determination of risk factors for CAD by multivariate logistic regression analysis

Potential CAD risk factors were determined by multivariate logistic regression (forward: conditional method). For the whole cohort, the variables in the multivariate model included: numerical data such as age, SBP, DBP, TCH, TG, FBG, HDL-c, LDL-c, LVDd, LVDs, LVEF, *E*, *A*, *E/A*, *e'*, *a'*, and *E/e'* and categorical data such as sex, smoking status, and drinking status. The results in Table 7 show that sex (OR, 0.202; 95% CI, 0.063–0.646, *p*=0.007), LDL-c (OR, 0.529; 95% CI, 0.285–0.984, *p*=0.044), *E/A* (OR, 0.176; 95% CI, 0.033–0.932, *p*=0.041), and *E/e'* (OR, 1.350; 95% CI, 1.087–1.676, *p*=0.007) continued to be independent risk factors for CAD in the study population.

Table 4. Receiver operating characteristic curve analyses in subjects with CHD and controls.

Variable	AUC(95%CI)	P value
E/e'	0.635 (0.515–0.755)	0.043
Age (years)	0.510 (0.369–0.650)	0.886
Sex (M/F)	0.614 (0.483–0.745)	0.087
SBP (mmHg)	0.583 (0.450–0.715)	0.216
DBP (mmHg)	0.595 (0.463–0.727)	0.156
Total cholesterol (mmol/L)	0.610 (0.483–0.737)	0.099
Triglycerides (mmol/L)	0.582 (0.454–0.710)	0.222
Glucose (mmol/L)	0.552 (0.422–0.683)	0.436
HDL-C (mmol/L)	0.651 (0.527–0.775)	0.024
LDL-C(mmol/L)	0.595 (0.468–0.723)	0.153
Smoking (yes *vs.* no)	0.578 (0.449–0.706)	0.246
Drinking (yes *vs.* no)	0.508 (0.377–0.640)	0.901
LVDd (mm)	0.645 (0.524–0.765)	0.031
LVDs (mm)	0.625 (0.50–0.751)	0.061
LVEF (%)	0.581 (0.455–0.706)	0.227
E (cm/s)	0.507 (0.378–0.636)	0.920
A (cm/s)	0.625 (0.491–0.760)	0.061
E/A	0.611 (0.473–0.749)	0.097
e'	0.643 (0.519–0.767)	0.032
a'	0.559 (0.423–0.696)	0.374

CI – confidence interval; AUC – area under the receiver operating characteristic curve; SBP – systolic blood pressure; DBP – diastolic blood pressure; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; CHD – coronary heart disease; LVDd – LV end-diastolic diameter; LVDs – LV end-systolic diameter; LVEF – LV ejection fraction, the peak velocity of early rapid filling; *A* – atrial filling velocity; *E/A* – E wave/A wave ratio; *e'* – the peak velocities during early diastole; *a'* – the peak velocities during late diastole; *E/e'* – mitral flow E wave velocity/lateral annular e' wave velocity by TDI. AUC >0.5 and p<0.05 indicates the levels in patients with CHD higher than in controls.
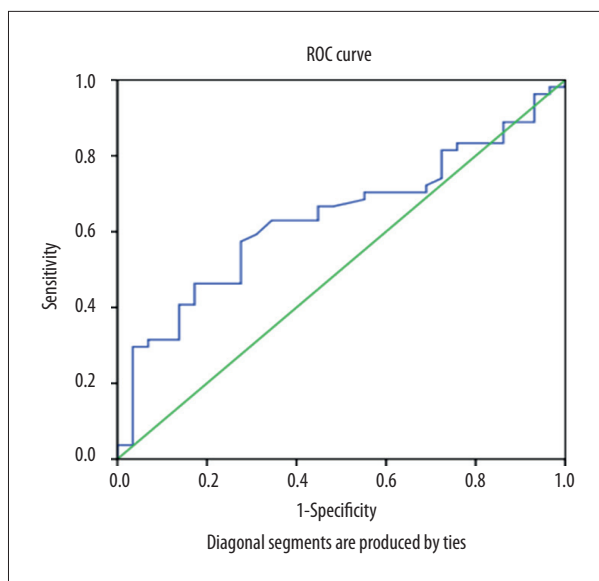
Figure 2. The receiver operating characteristic curve for the ability of *E/e'* to differentiate the CHD cases from the control individuals.
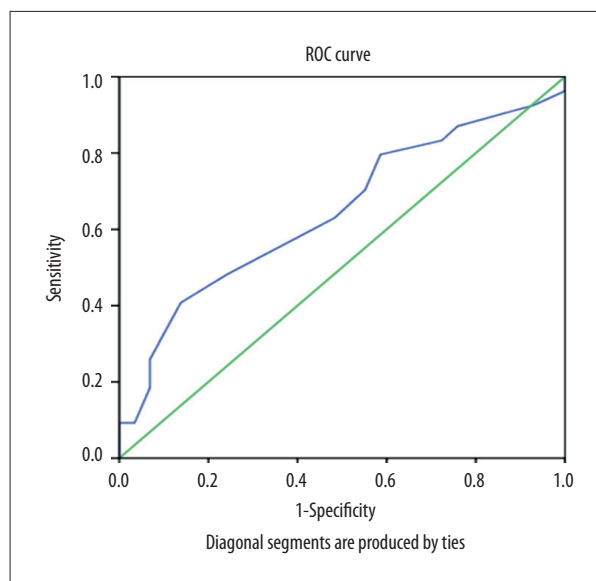

Figure 4. The receiver operating characteristic curve for the ability of LV end-diastolic diameter to differentiate the CHD cases from the control individuals.
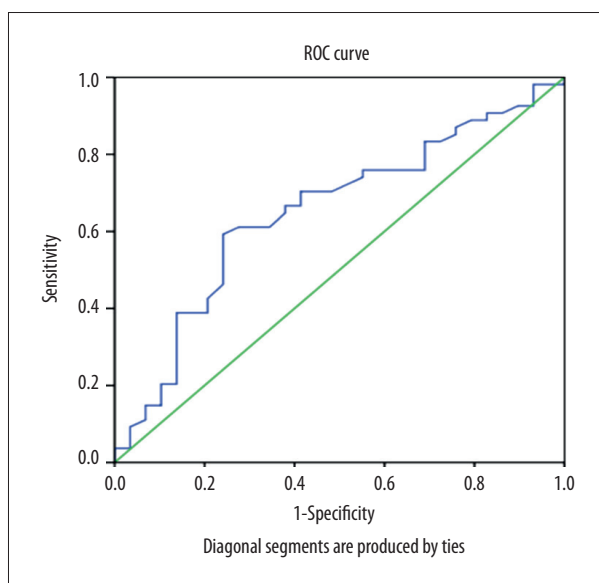

Figure 3. The receiver operating characteristic curve for the ability of fasting high-density lipoprotein cholesterol to differentiate the CHD cases from the control individuals.
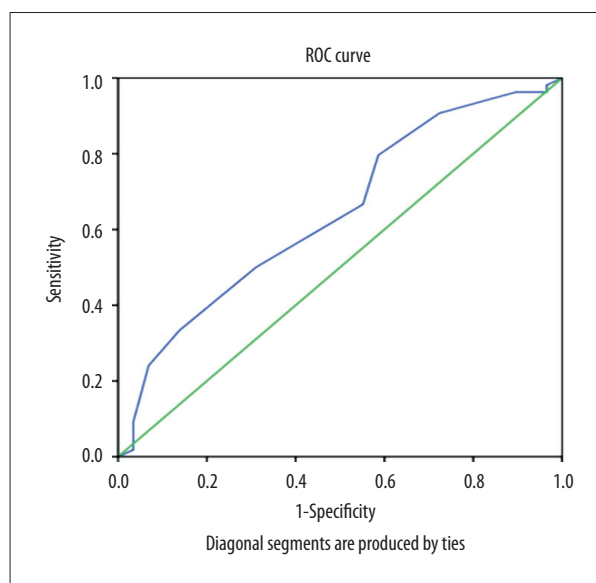

Figure 5. The receiver operating characteristic curve for the ability of the peak velocities during early diastole to differentiate the CHD cases from the control individuals.

Discussion

The present study demonstrated the following major findings: 1) the E/e' ratio differed significantly between CAD patients and control participants, and thus was closely associated with CAD; and 2) the *E/e'* ratio is a simple and practical predictor of CAD with an optimum cut-off point of 8.153 resulting in a specificity of 72.4% and sensitivity of 57.4%.

To investigate the correlation between the *E/e'* and CAD, we performed a multivariate logistic regression analysis to identify whether *E/e'* was an independent predictor for CAD in our study population. After refinement for other risk factors, we found that the risk of developing CAD increased by 35.0% with every quartile increase in *E/e'* (OR, 1.350; 95% CI, 1.087–1.676, p=0.007). Thus, our findings indicate that the *E/e'* ratio may be an independent predictor of CAD.

Table 5. The optimal cut-off and the Youden index of *E/e'* and traditional risk factor.

Variables	Cut-off	Sensitivity	Specificity	Youden index
E/e'	8.153	0.574	0.724	0.298
HDL-C (mmol/L)	0.995	0.593	0.759	0.352
LVDd (mm)	50.5	0.407	0.862	0.269
e'	0.105	0.796	0.414	0.210

E/e' – mitral flow *E* wave velocity/lateral annular e' wave velocity by TDI; HDL-C – high-density lipoprotein cholesterol; LVDd – LV end-diastolic diameter; *e'* – the peak velocities during early diastole.

Table 6. Univariate logistic regression for the presence of obstructive CHD.

Characteristic	All subjects			
	B	*OR*	95%CI	*P*
Age (years)	0.001	1.001	0.961; 1.042	0.966
Sex (male=1; female=2)	−1.133	0.322	0.117; 0.883	0.028
Smoking status (yes=1; no=0)	0.642	1.900	0.747; 4.831	0.178
Drinking status (yes=1; no=0)	−0.085	0.919	0.332; 2.539	0.870
SBP (mmHg)	0.011	1.011	0.996; 1.026	0.163
DBP (mmHg)	0.018	1.018	0.994; 1.041	0.137
Total cholesterol (mmol/L)	−0.269	0.764	0.506; 1.153	0.200
Triglycerides (mmol/L)	0.275	1.317	0.809; 2.142	0.268
Glucose (mmol/L)	0.197	1.218	0.865; 1.715	0.259
HDL-C (mmol/L)	−1.632	0.196	0.038; 1.009	0.051
LDL-C (mmol/L)	−0.367	0.693	0.409; 1.176	0.174
LVDd (mm)	0.145	1.157	1.011; 1.323	0.034
LVDs (mm)	−0.008	0.992	0.973; 1.011	0.387
LVEF (%)	−0.079	0.924	0.825; 1.036	0.175
E (cm/s)	0.117	1.124	0.055; 22.859	0.940
A (cm/s]	2.099	8.161	0.729; 91.385	0.089
E/A	−1.432	0.239	0.053; 1.082	0.063
e'	−21.072	0.000	0.000; 0.312	0.038
a'	−11.261	0.000	0.000; 307.2	0.253
E/e'	0.183	1.201	0.998; 1.444	0.053

CHD – coronary heart disease; HDL-c – fasting high-density lipoprotein cholesterol; LDL-c – fasting low-density lipoprotein cholesterol; SBP – systolic blood pressure; DBP – diastolic blood pressure; LVDd – LV end-diastolic diameter; LVDs – LV end-systolic diameter; LVEF – the LV ejection fraction; *E* – the peak velocity of early rapid filling; *A* – atrial filling velocity; *E/A* – E wave/A wave ratio; *e'* – the peak velocities during early diastole; *a'* – the peak velocities during late diastole; *E/e'* – mitral flow E wave velocity/lateral annular *e'* wave velocity by TDI.

Table 7. Multivariate logistic regression for the presence of obstructive CHD.

Characteristic	All subjects			
	B	OR	95% CI	P
Sex (male=1; female=2)	−1.598	0.202	0.063, 0.646	0.007
LDL-C (mmol/L)	−0.636	0.529	0.285, 0.984	0.044
E/A	−1.740	0.176	0.033; 0.932	0.041
E/e'	0.300	1.350	1.087, 1.676	0.007

CHD – coronary heart disease; LDL-c – fasting low-density lipoprotein cholesterol; *E/A* – E wave/A wave ratio; *E/e'* – mitral flow E wave velocity/lateral annular *e'* wave velocity by TDI.

According to the recommendations of the ASE and ESC, an $E/e'_{lateral}$ >12, E/e'_{mean} >13, and E/e'_{septal} >15 represent an elevated LVFP and diastolic dysfunction, whereas an *E/e'* <8 represents normal LVFP and diastolic function. If *E/e'* is >8 but <12–15, another echocardiographic index is needed for appraisal of LVFP and diastolic function [8,9]. ROC curve analysis in the present study showed that the optimal cut-off for the *E/e'* ratio was 8.153 for the prediction of CAD, and the corresponding specificity and sensitivity values were 72.4% and 57.4%, respectively. These findings are in agreement with those of previous studies. Moreover, the present study suggests that an *E/e'* <8 is not only an indicator of normal LVFP and diastolic function, but also may be an indicator of CAD.

An advantage of our investigation is that coronary angiography and echocardiography were used for the assessment of CAD and the *E/e'* ratio, respectively. However, several limitations were present in this investigation and need to be acknowledged. For example, our study had a small sample size; hence, studies in large cohorts are needed to confirm our observations. Furthermore, due to the cross-sectional design of our study, we cannot infer definite cause-effect relationships. Finally, the pathogenesis of the overt correlation between the

E/e' ratio and CAD was not explored; therefore, the underlying mechanisms explaining how the *E/e'* ratio can predict CAD warrant further investigation in the future.

Conclusions

In summary, we have identified the *E/e'* ratio as a simple and practical predictor of CAD, and our results indicate that the *E/e'* ratio can serve as an independent risk factor for diagnosing CAD. Future studies in large cohorts are required to confirm our observations.

Conflict of interest

None.

Acknowledgments

References:

1. Redfield MM, Jacobsen SJ, Burnett JC Jr. et al: Burden of systolic and diastolic ventricular dysfunction in the community: Appreciating the scope of the heart failure epidemic. JAMA, 2003; 289: 194–202

2. Owan TE, Hodge DO, Herges RM et al: Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med, 2006; 355: 251–59

3. Kane GC, Karon BL, Mahoney DW et al: Progression of left ventricular diastolic dysfunction and risk of heart failure. JAMA, 2011; 306: 856–63

4. Kasner M, Westermann D, Steendijk P et al: Utility of Doppler echocardiography and tissue Doppler imaging in the estimation of diastolic function in heart failure with normal ejection fraction: A comparative Doppler-conductance catheterization study. Circulation, 2007; 116: 637–47

5. Edelmann F, Wachter R, Schmidt AG et al: Effect of spironolactone on diastolic function and exercise capacity in patients with heart failure with preserved ejection fraction: The Aldo-DHF randomized controlled trial. JAMA, 2013; 309: 781–91

6. Kim YH, Kim SH, Lim SY et al: Relationship between depression and subclinical left ventricular changes in the general population. Heart, 2012; 98: 1378–83

7. Ohtani T, Mohammed SF, Yamamoto K et al: Diastolic stiffness as assessed by diastolic wall strain is associated with adverse remodelling and poor outcomes in heart failure with preserved ejection fraction. Eur Heart J, 2012; 33: 1742–49

8. Nagueh SF, Appleton CP, Gillebert TC et al: Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr, 2009; 22: 107–33

9. McMurray JJ, Adamopoulos S, Anker SD et al: ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J, 2012; 33: 1787–847

10. Bonow RO, Bacharach SL, Green MV et al: Impaired left ventricular diastolic filling in patients with coronary artery disease: Assessment with radionuclide angiography. Circulation, 1981; 64: 315–23

11. Inouye I, Massie B, Loge D et al: Abnormal left ventricular filling: An early finding in mild to moderate systemic hypertension. Am J Cardiol, 1984; 53: 120–26

12. Hillis GS, Moller JE, Pellikka PA et al: Noninvasive estimation of left ventricular filling pressure by E/e' is a powerful predictor of survival after acute myocardial infarction. J Am Coll Cardiol, 2004; 43: 360–67

13. Kurisu S, Iwasaki T, Ikenaga H et al: Association of mitral annular velocity with myocardial ischemia assessed by single-photon emission computed tomography in patients with suspected coronary artery disease and preserved ejection fraction. Nucl Med Commun, 2016; 37: 278–82

14. Fukuta H, Ohte N, Wakami K et al: Prognostic value of left ventricular diastolic dysfunction in patients undergoing cardiac catheterization for coronary artery disease. Cardiol Res Pract, 2012; 2012: 243735

15. Jia EZ, An FH, Liu P et al: Relationship between brachial-ankle pulse wave velocity and cardiovascular risk factors: A multi-ethnic study. Intern Med, 2012; 51: 537–43

16. Judkins MP: Selective coronary arteriography. I. A percutaneous transfemoral technic. Radiology, 1967; 89: 815–24

17. Sun X, Zhang M, Sanagawa A et al: Circulating microRNA-126 in patients with coronary artery disease: Correlation with LDL cholesterol. Thromb J, 2012; 10: 16

18. Gensini GG: A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol, 1983; 51: 606

19. Porter TR, Shillcutt SK, Adams MS et al: Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: A report from the American Society of Echocardiography. J Am Soc Echocardiogr, 2015; 28: 40–56

20. Rychik J, Ayres N, Cuneo B et al: American Society of Echocardiography guidelines and standards for performance of the fetal echocardiogram. J Am Soc Echocardiogr, 2004; 17: 803–10

21. Alam M, Wardell J, Andersson E et al: Characteristics of mitral and tricuspid annular velocities determined by pulsed wave Doppler tissue imaging in healthy subjects. J Am Soc Echocardiogr, 1999; 12: 618–28

22. Hanley JA, McNeil BJ: The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology, 1982; 143: 29–36