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Research article

Prevalence of stable coronary artery disease and its associated clinical factors among patients with chest pain and elevated cardiac troponin alone

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ABSTRACT

Cardiac troponin is a useful test for diagnosing cardiogenic causes in patients with chest pain. However, cardiac troponin levels are often elevated in patients with chest pain due to non-cardiac causes other than coronary artery disease. The purpose of this study was to investigate the prevalence of coronary artery disease (CAD) and its associated factors in patients with chest pain and elevated cardiac troponin I (cTnI). 104 patients (mean age, 65 ± 11 years; 60 [58%] men) who underwent coronary angiography (CAG) for chest pain and elevated cTnI levels were enrolled in this study. All patients had a normal CK-MB range and did not show any ischemic changes on electrocardiography or echocardiography. Patients were classified into two groups according to the presence of CAD (Group 1, n = 62) and the absence of CAD (Group 2, n = 42). Patients were classified into subgroups according to the presence (Group 2a, microvascular angina [MVA], n = 18) and absence (Group 2b, non-angina [NA], n = 25) of angina. CAD was diagnosed in 62 (60%) patients and MVA was suspected in 18 (17%) patients without CAD. Patients with CAD showed elevated blood pressure and slightly decreased heart rate. Diabetes mellitus was more prevalent in patients with CAD and patients without CAD (esp. with MVA) were more likely to be common drinkers. Increased relative wall thickness (RWT) and reduced E' velocity were associated with CAD. High-density lipoprotein (HDL) levels were reduced in patients with CAD and MVA but were higher in patients with NA. Lower HDL level was found to be independently associated with the presence of CAD. Elevated cTn1 levels without other evidence of myocardial ischemia are sufficient for performing CAG in patients with stable chest pain.

1. Introduction

Chest pain is one of the most common symptoms requiring medical care, especially in emergency departments [1]. In cases of life-threatening conditions associated with chest pain, such as acute coronary syndrome (ACS) [2,3], acute aortic syndrome [4], pulmonary thromboembolism (PTE) [5], tension pneumothorax [6], pericardial tamponade [7], or mediastinitis (especially due to esophageal rupture) [8], proper treatment – invasive or non-invasive – must be implemented promptly to save the patient's life. Other common causes that are not life-threatening include gastrointestinal problems, such as gastroesophageal reflux disease (GERD) [2]),

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musculoskeletal causes [9], psychiatric causes (DSM-5, 2013), and other less common causes. It is very important to differentiate between ACS and other causes of chest pain, life-threatening or non-cardiac causes, and to perform coronary angiography (CAG) or percutaneous coronary intervention (PCI) in patients who require it.

ACS occurs due to atherosclerotic plaque rupture, and thrombus formation results from adhesion, activation, and aggregation of platelets, which reduces coronary blood flow and causes myocardial ischemia [10]. The degree and duration of the oxygen supply-demand mismatch depends on the presence or absence of myocardial injury, and determines whether the patient develops unstable angina (UA) or myocardial infarction (MI) [11]. The role of cardiac biomarkers, especially cardiac troponin, is very important for diagnosing or excluding ACS in patients with chest pain without ST elevation on ECG [12]. In addition, cardiac troponin is useful for the differential diagnosis of suspected non-ST-segment elevation MI (NSTEMI). Patients presenting with ST-segment elevation MI require immediate intervention based on the current guidelines, even before their cardiac troponin results are available [13].

There have been many reports of an increase in cardiac troponin even in non-MI situations, including situations mimicking MI, such as spontaneous coronary artery dissection [14], stress-induced cardiomyopathy (CMP) [15], and non-ACS related situations (including chronic renal failure and heart failure (HF) [15], and severe sepsis [16]. Type 2 MI can be considered in situations outside of traditional MI, and is defined as MI secondary to ischemia due to either increased oxygen demand or decreased supply [13].

However, some patients with chest pain and elevated cardiac troponin levels are not eligible for ACS without evidence of myocardial ischemia in tests such as cardiac biomarkers, ECG, and echocardiography. There have been some reports that patients with stable angina can have chronic elevations of cardiac troponin [17–19], so cardiac troponin elevation may not be limited to acute MI. In addition, many clinical conditions are associated with cardiomyocyte injury with elevated cardiac troponin levels [20]. Therefore, we enrolled patients with stable chest pain and elevated cardiac troponin levels without evidence of myocardial ischemia to evaluate the prevalence of coronary artery disease (CAD) and its related clinical factors.

2. Methods

2.1. Study design and participants

This was a cross-sectional study of 104 patients who underwent CAG for the evaluation of chest pain and elevated cardiac troponin levels (60 [58%] men, mean age: 65 ± 11 years). We only included patients who showed normal left ventricular (LV) systolic function without regional wall motion abnormality (RWMA) on echocardiography, without elevation of creatine kinase-MB (CK-MB) or ST change on electrocardiogram (ECG). Patients attended our hospital between January 2019 and March 2022. We excluded patients with CMP, pre-existing HF, previous coronary stents, cardiac devices, significant arrhythmia (including AV block), valvular diseases, pericardial disease, PTE, cardiac tumor (mass) or IE, acute cerebrovascular attack (CVA), hyperthyroidism, severe lung or airway diseases (asthma or chronic obstructive pulmonary disease; COPD), severe sepsis, and cardiac arrest or suspicion of ACS.

All procedures were performed in accordance with the ethical standards of the Institutional Research Committee and the 1964 Declaration of Helsinki and its later amendments. The need for informed consent was waived owing to the retrospective design of this study. The authors had no access to information that could potentially identify the patients.

2.2. Coronary angiography (CAG)

CAG was performed according to the current guidelines of board-certified cardiologists [21]. Patients with obstructive CAD were treated according to contemporary guidelines [22,23]. Normal coronary arteries (absence of CAD) were defined as 0% luminal stenosis or <20% stenosis [24]. Significant coronary artery obstruction was defined as >70% luminal stenosis, and 20–70% luminal stenosis was defined as intermediate lesion [25,26]. Coronary revascularization (PCI or coronary artery bypass graft; CABG) was performed in patients with significant stenosis or in patients with >50–70% luminal stenosis if associated with inducible ischemia or fractional flow reserve ≤0.08 [27]. Antianginal medications were administered to patients with intermediate lesions. Variant angina (VA) was diagnosed using the ergonovine provocation test during CAG, defined as transient total or subtotal coronary artery occlusion (>90% constriction) with angina and ischemic ECG changes [28]. The presence of CAD was defined as significant obstruction, intermediate lesions, or VA. Microvascular angina (MVA) was diagnosed in patients without CAD but typical chest pain with improvement after medications, including nitroglycerin [29]. Non-angina (NA) was defined as the absence of CAD and MVA but suspected non-cardiac causes of chest pain and elevated cardiac troponin I (cTnI) alone.

2.3. Classification of the participants

Patients were classified into two categories according to their coronary angiography results (Group 1: with CAD, n = 62 [60%] vs. Group 2: without CAD, n = 42 [40%]). Clinical, laboratory, and echocardiographic parameters were compared between the two groups.

1. Group 1: Patients with CAD (intermediate lesion, significant obstruction, and variant angina) = 62 (60%)
2. Group 2: Patients without CAD = 42 (40%)

Patients were further divided into three groups according to their CAD diagnosis (patients with MVA or without angina).

1. Group 1: Patients with CAD = 62 (60%)
2. Group 2a: Patients with MVA = 17 (16%)
3. Group 2b: Patients without angina (non-angina; NA) = 25 (24%)

2.4. Transthoracic echocardiography

Transthoracic echocardiography (TTE) was performed using standard techniques with a 2.5-MHz transducer. TTE was performed by a well-trained sonographer (with over 6 months of experience), and the results were confirmed by a cardiologist almost in real time. Standard 2-dimensional (2-D) and Doppler echocardiography were performed using a commercially available echocardiographic machine (Vivid 7R; GE Medical System, Horten, Norway) with the same setup and interfaced with a 2.5-MHz phased-array probe. All measurements were performed in accordance with the guidelines [30]. With the study participant in the partial left decubitus position and breathing normally, the observer obtained images from the parasternal long and short axes, and from the apical four- and two-chamber and long-axis views. The depth setting was optimized to display the left ventricle as large as possible on the screen, and the same field depth was maintained for the four- and two-chamber apical views. The sector width was reduced to increase the spatial and temporal resolution. Left ventricular end-diastolic dimensions (LVEDD), end-diastolic interventricular septal thickness (IVSTs), and end-diastolic LV posterior wall thickness (PWTd) were measured at end-diastole according to the standards established by the American Society of Echocardiography. LV ejection fraction (EF) was determined using the biplane Simpson's method. The maximal left atrial (LA) volume was calculated using the Simpson method and indexed to the body surface area. LV mass was calculated using the Devereux formula as $1.04\ [(\mathrm{LVEDD} + \mathrm{IVSTd} + \mathrm{PWTd})^3 - (\mathrm{LVEDD})^3] - 13.6$. Thereafter, the left ventricular mass index (LVMI) was calculated and indexed to the body surface area.

The mitral flow velocities were recorded in the apical four-chamber view. Mitral inflow measurements included the peak early (E) and peak late (A) flow velocities and E/A ratio. Tissue Doppler of mitral annulus movement was also obtained from the apical four-chamber view. A 1.5-mm sample volume was placed sequentially at the septal annular sites. The analysis was performed for early diastolic (E′), late diastolic (A′), and systolic (S′) peak tissue velocities. As a non-invasive parameter for the LV stiffness, the LV filling index (E/E') was calculated as the ratio of transmitral flow velocity to annular velocity. Adequate mitral and tissue Doppler image signals were recorded for all the patients.

2.5. Statistical analysis

All continuous data are expressed as mean ± SD, and all categorical data are presented as percentages or absolute numbers. Continuous variables were analyzed using one-way ANOVA in three independent groups, Student's t-test in two independent groups, and dichotomous variables were analyzed using the chi-square test. Non-normally distributed variables were analyzed using the

Table 1
Baseline clinical characteristics of the study population.

	CAD (n = 62)	No CAD (n = 42)	p
Age (years)	65 ± 11	63 ± 12	0.137
Male gender	35 (57%)	25 (60%)	0.841
SBP (mmHg)	134 ± 25	125 ± 16	0.047
DBP	75 ± 12	76 ± 10	0.792
Heart rate (bpm)	67 ± 11	73 ± 12	0.034
Body mass index (kg/m^2)	26.0 ± 3.4	25.4 ± 3.4	0.327
DM	21 (34%)	6 (14%)	0.039
Hypertension	40 (65%)	22 (52%)	0.229
Smoking	12 (19%)	11 (26%)	0.474
Alcohol drinker	12 (19%)	17 (41%)	0.026
Medications			0.120
APT	19 (31%)	10 (24%)	0.509
RASB	27 (44%)	10 (24%)	0.060
CCB	26 (42%)	15 (36%)	0.547
BB	7 (11%)	4 (10%)	1.000
Statin	30 (48%)	16 (38%)	0.322
Treatment			
PCI	41 (66%)		
CABG	5 (8%)		
Medical	16 (26%)		
Lesion			
1 VD	41 (66%)		
2 VD	13 (21%)		
3 VD	6 (10%)		
VA	2 (3%)		

CAD, coronary artery disease; SBP and DBP, systolic and diastolic blood pressure; DM, diabetes mellitus; APT, antiplatelet therapy; RASB, renin-angiotensin system blocker; CCB, calcium channel blocker; BB, beta blocker; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; VD, vessel disease.

Kruskal-Wallis test or the Mann-Whitney *U* test. Cox regression analysis was performed to evaluate significant variables associated with CAD. Statistical significance was set at $p < 0.05$. All tests were performed using SPSS, version 18.0 (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Comparison of baseline characteristics of the study population and results of CAG (Table 1)

CAD was diagnosed in 62 (60%) of 104 patients, and among these, 41 (66%) underwent PCI, five (8%) underwent CABG, and 16 (26%) received medical management. Patients with CAD had elevated systolic blood pressure (SBP) (134 ± 26 vs. 125 ± 16 mmHg, $p = 0.047$) and a slightly decreased heart rate (HR) (67 ± 11 vs. 73 ± 12 beats/min, $p = 0.034$). Diabetes mellitus (DM) was more prevalent in patients with CAD (34 vs. 14%, $p = 0.039$), current drinkers were more common in patients without CAD (20 vs. 41%, $p = 0.026$).

3.2. Echocardiographic and laboratory findings of the study population (Tables 2 and 3)

There were no significant differences in the echocardiographic parameters of the study population. However, relative wall thickness (RWT) was higher in patients with CAD than in those without (0.43 ± 0.07 vs. 0.40 ± 0.06, $p = 0.014$). CAD patients also showed a reduced E′ velocity (6.1 ± 2.2 vs. 7.3 ± 2.8 cm/s, $p = 0.017$) and E'/A' ratio (0.64 ± 0.24 vs. 0.78 ± 0.31, $p = 0.015$) than those without CAD.

In laboratory findings, the mean cTnI level was 276.72 ng/dL (31.9–3322.0 ng/dL), and there was no difference in cTnI or other cardiac biomarkers. However, high density lipoprotein (HDL) was reduced in patients with CAD (45.0 ± 10.3 vs. 55.3 ± 19.3, $p = 0.004$).

3.3. Independent predictors for CAD in patients with chest pain and elevated cardiac troponin (Table 4)

The presence of DM, increased RWT, decreased E' velocity, and reduced HDL levels were found to be associated with CAD in the univariate analysis. However, current alcohol consumption was more prevalent with patients without CAD. Among them, lower HDL (OR: 0.937, 95% CI: 0.894–0.981, $p = 0.005$) was found to be independently associated with the presence of CAD..

3.4. Sub-group analysis of patients with CAD, MVA, and NA (Table 5)

HR was lowest in patients with CAD and highest in patients with NA (67 vs. 70 vs. 74 bpm in order, $p = 0.056$). Interestingly, the number of current alcohol drinkers was the lowest amongst patients with CAD and the highest amongst patients with MVA (19% vs. 47% vs. 36%, $p = 0.046$). DM was most frequent in patients with CAD, followed by patients with MVA, and least frequent in patients with NA (34%, 24%, and 8%, respectively; $p = 0.044$).

Among echocardiographic parameters, RWT was the highest in patients with CAD and the lowest in patients with MVA (0.43 vs.

Table 2
Echocardiographic parameters of study population.

	CAD (n = 62)	No CAD (n = 42)	p
LAVI (ml/m^2)	27.9 ± 9.9	27.9 ± 11.7	0.992
LV EDD (mm)	48.1 ± 4.8	47.9 ± 8.7	0.857
LV ESD (,_	30.6 ± 3.5	32.4 ± 6.9	0.078
LVMI (g/m^2)	105.4 ± 23.7	102.7 ± 22.3	0.550
RWT	0.43 ± 0.07	0.40 ± 0.06	0.014
LV EF (%)	65.7 ± 5.6	64.9 ± 6.2	0.506
E (cm/s)	61.8 ± 13.5	64.6 ± 23.8	0.446
A (cm/s)	82.1 ± 16.9	77.2 ± 15.5	0.154
E/A ratio	0.76 ± 0.23	0.82 ± 0.30	0.338
DT (ms)	228.9 ± 45.3	227.0 ± 65.8	0.863
E' (cm/s)	6.1 ± 2.2	7.3 ± 2.8	0.017
A' (cm/s)	9.8 ± 2.4	9.3 ± 1.7	0.289
E'/A'	0.64 ± 0.24	0.78 ± 0.31	0.015
E/E'	11.0 ± 3.4	9.8 ± 4.3	0.126
S' (cm/s)	7.7 ± 1.9	7.9 ± 1.7	0.721
RVSP (mmHg)	29.0 ± 7.6	28.8 ± 5.2	0.842
Diastolic grade			0.150
Normal	5 (9%)	8 (22%)	
Grade 1	53 (90%)	27 (75%)	
Grade 2	1 (1%)	1 (3%)	

LAVI, left atrial volume index; LV, left ventricular; EDD, end-diastolic dimension; ESD, end-systolic dimension; LVMI, LV mass index; RWT. Relative wall thickness; EF, ejection fraction; GS, global strain; DT, deceleration time; RVSP: right ventricular systolic pressure.

Table 3
Laboratory parameters of study population.

	CAD (n = 62)	No CAD (n = 42)	p
Troponin I (pg/mL)	277.0 ± 480.1	271.0 ± 425.5	0.948
CK (μg/dL)	137.9 ± 121.1	122.3 ± 67.1	0.450
CK-MB (ng/mL)	2.89 ± 4.54	3.08 ± 1.95	0.455
BNP (pg/mL)	97.5 ± 118.8	124.7 ± 205.7	0.454
GFR (mL/mib/1.73m^2)	76.3 ± 18.0	79.0 ± 19.5	0.472
TC (mg/dL)	161.2 ± 42.4	166.0 ± 42.7	0.576
LDL (mg/dL)	90.8 ± 32.1	97.2 ± 33.7	0.351
HDL (mg/dL)	45.0 ± 10.3	55.3 ± 19.3	0.004
TG (mg//dL)	170.4 ± 96.2	154.8 ± 120.8	0.840
*TG (mg/dL)	115 (30–458)	135 (24–1575)	0.401
*CK-MB (ng/mL)	1.05 (0.18–20.39)	1.15 (0.02–34.19)	0.782
TSH (μIU/mL)	2.61 ± 4.51	1.67 ± 1.26	0.200
fT4 (ng/dL)	1.23 ± 0.24	1.19 ± 0.21	0.367

CK, creatine kinase; BNP, brain natriuretic peptide; GFR, glomerular filtration rate; TC, total cholesterol; LDL, low density lipoprotein; TG. triglycerides; TSH, thyroid stimulating hormone; fT4, free thyroxine 4. * Analyzed by Mann-Whitney *U* test and data are expressed as median (IQR).

Table 4
Independent predictors for CAD in patients with chest pain and elevated cardiac troponin.

	OR	95% CI	P
Univariate			
SBP	1.022	1.000–1.045	0.055
HR	0.982	0.939–1.027	0.437
DM	3.073	1.117–8.452	0.030
Alcohol	0.353	0.146–0.852	0.021
RWT	1.081	1.014–1.153	0.018
E′	0.820	0.691–0.973	0.023
HDL	0.940	0.903–0.977	0.002
Multivariate			
DM	2.024	0.621–6.596	0.242
alcohol	0.518	0.187–1.439	0.207
RWT	1.077	0.998–1.163	0.057
E′	0.901	0.783–1.100	0.306
HDL	0.942	0.903–0.984	0.007

OR, odds ratio; CI, confidence interval; SBP and DBP, systolic and diastolic blood pressure; HR, heart rate; DM, diabetes mellitus; RWT, relative wall thickness; E′, E′ velocity; HDL, high density lipoprotein.

Table 5
Subgroup analysis of patients with CAOD, MVA and NA.

	CAD (n = 62)	MVA (n = 17)	NA (n = 25)	p
Age (years)	66 ± 11	65 ± 11	61 ± 13	0.105
Male	35 (57%)	11 (61%)	14 (56%)	0.943
SBP (mmHg)	134 ± 25	122 ± 18	127 ± 14	0.105
DBP (mmHg)	75 ± 12	73 ± 9	78 ± 10	0.460
HR (bpm)	67 ± 11	70 ± 10	74 ± 14	0.056
Alcohol	12 (19%)	8 (47%)	9 (36%)	0.046
DM	21 (34%)	4 (24%)	2 (8%)	0.044
LAVI (ml/m^2)	27.9 ± 9.9	25.2 ± 6.6	29.7 ± 14.0	0.392
LVMI (gl/m^2)	105.7 ± 23.8	101.7 ± 19.8	102.8 ± 24.0	0.836
RWT	0.43 ± 0.08	0.38 ± 0.0.8	0.41 ± 0.07	0.033
LV EF (%)	65.6 ± 5.7	66.8 ± 5.3	63.6 ± 6.3	0.182
LV GS (%)	−16.6 ± 3.6	−18.9 ± 3.0	−17.0 ± 3.8	0.070
E' (cm/s)	6.1 ± 2.1	7.3 ± 2.7	7.3 ± 2.9	0.060
A' (cm/s)	9.6 ± 2.1	10.2 ± 2.8	9.0 ± 1.7	0.240
E/E'	7.6 ± 1.6	8.5 ± 2.4	7.8 ± 1.8	0.159
BNP (pg/mL)	97.5 ± 118.8	40.0 ± 35.4	196.0 ± 259.2	0.011
TnI (pg/mL)	277.0 ± 480.1	334.8 ± 421.6	274.6 ± 456.7	0.759
HDL (mg/dL)	45.0 ± 10.5	50.0 ± 12.0	59.4 ± 22.8	0.001
TSH (μIU/mL)	2.64 ± 4.56	1.62 ± 1.34	1.69 ± 1.19	0.415

CAD, coronary artery disease; MVA, microvascular angina; NA, non-angina; SBP and DBP, systolic and diastolic blood pressure; HR, heart rate; DM, diabetes mellitus; LAVI, left atrial volume index; LMVI, left ventricular mass index; RWT, relative wall thickness; EF, ejection fraction; GS, global strain; BNP, brain natriuretic peptide; HDL, high density lipoprotein; TSH, thyroid stimulating hormone.

0.38 vs. 0.41, respectively; $p = 0.033$). There were no significant differences in terms of either systolic or diastolic parameters among the study populations; however, global stain (GS) was lower in patients with CAD and NA and higher in patients with MVA. The E′ velocity was the lowest and E/E' was the highest in patients with CAD, with marginal statistical significance.

Levels of cTnI did not differ among the three groups. Brain natriuretic peptide (BNP) levels were the highest in patients with NA and the lowest in patients with MVA (98 vs. 40 vs. 196 pg/mL, $p = 0.011$). HDL levels were the lowest in patients with CAD and the highest in patients with NA (45 vs. 50 vs. 59 mg/dL, $p = 0.001$).

Fig. 1 shows the differences in the prevalence of DM (Fig. 1-A: the DM rate was highest in the CAD group and the lowest in the NA group) and current alcohol drinkers. (Fig. 1-B: the difference in the proportion of drinkers between the three groups. The rate of drinkers was the highest in the MVA group and the lowest in the CAD group).

Fig. 2 shows the relationship between BNP, HR, HDL, and GS in patients with CAD, MVA, and NA. (2-A: the BNP level was the highest in the NA group and the lowest in the MVA group, 2-B: HR was the highest in the NA group and lowest in the CAD group, 2-C: the HDL level was the lowest in the CAD group and the highest in the NA group, and 2-D: GS was the highest in the MVA group and lowest in the CAD group).

4. Discussion

In this study, CAD was diagnosed in 61 (59%) patients with chest pain and elevated cardiac TnI only, without elevation of CK-MB, ECG change, or RWMA by TTE. MVA was diagnosed in 18 (43%) patients without CAD using CAG (no CAD, n = 42). Decreased HR, increased RWT, and lower HDL levels were found to be independently associated with the presence of CAD in patients with chest pain and elevated cardiac TnI levels. In subgroup analysis of the three groups (CAD, MVA, and NA), patients with CAD showed elevated RWT, and E' velocity, and lower levels of HDL. Patients with MVA showed the most favorable echocardiographic parameters and the lowest BNP levels but lower HDL levels. Patients with NA showed the highest BNP and HDL levels.

When a patient has chest pain, it is necessary to carefully examine the characteristics of pain, pressure, tightness, or discomfort often associated with radiating pain to the shoulders, arms, neck, back, upper abdomen, or jaw and shortness of breath, and to exclude ACS if the symptoms are acute and indicative of angina [31]. Emergent CAG or PCI must be considered in patients with STEMI according to the current guidelines [13], and performing CAG within 72 h according to the patient's relevant comorbidity, evidence of recurrent ischemia (recurrence of symptoms or a positive ECG), or positive stress test [32] is recommended when managing ACS in patients without ST elevation.

If there is diffuse ST elevation consistent with pericarditis or no ST change elevation on the electrocardiogram, other diagnostic tests should be performed to differentiate the following diseases: NSTEMI or UA, acute aortic syndrome, pulmonary embolism, acute myopericarditis, or significant valvular heart diseases [32]. Among several tests to rule out specific diseases, the preferred biomarker to detect or exclude cardiac injury is cTnI because of its high sensitivity and specificity for myocardial tissue [33]. The definition of acute MI (type 1, 2, and 3 MI, excluding procedure-related MI) is a rise and/or fall in cTnI values within at least one value above the 99th percentile upper reference limit (URL), and at least one indication of myocardial ischemia, including acute symptoms, new ischemic ECG changes, development of pathologic Q waves, imaging evidence of new loss of viable myocardium, new RWMA in a pattern consistent with an ischemic etiology, or identification of a coronary thrombus [33]. TTE is very helpful in detecting RWMA consistent with AMI, and aids in the differential diagnosis among the numerous causes of acute chest pain, such as acute aortic dissection, pericardial effusion, stress cardiomyopathy, and hypertrophic cardiomyopathy [33,34]. Therefore, it is necessary to judge the patient's risk according to these results and perform invasive CAG in high-risk patients [32]. In the case of intermediate risk, additional tests should be performed in accordance with the clinical decision pathway (CDP) [32].

At this time, deciding whether to perform invasive CAG to detect CAD is still a problem that raises concern amongst clinicians due to its invasiveness and related complications. One study recommended performing a more precise pre-test before CAG [34], since more than half of the patients with acute chest pain suspected of UA did not need CAG. Therefore, we investigated the prevalence and

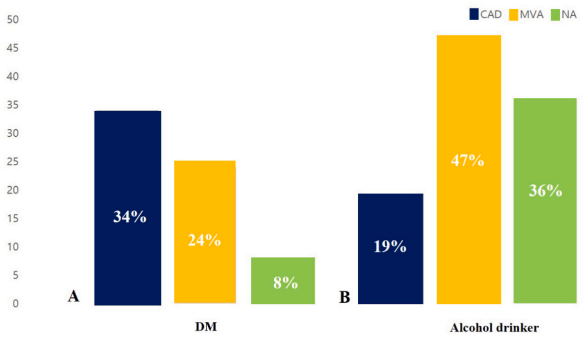

Fig. 1. A shows the difference in the prevalence of DM between the three groups. A: The DM rate was the highest in the CAD group and the lowest in the NA group. B: The difference in the proportion of drinkers between the three groups. The rate of drinkers was the highest in the MVA group and the lowest in the CAD group. DM, diabetes mellitus; CAD, coronary artery disease; NA, non-angina; MVA, microvascular angina.

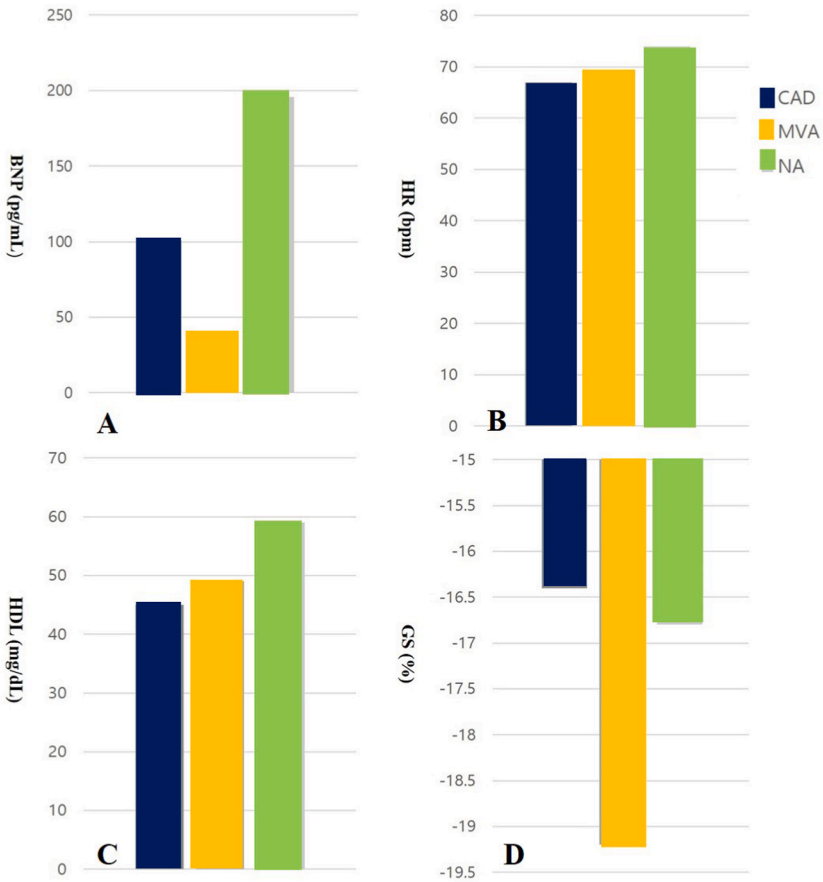

Fig. 2. Correlation of BNP (A), HR (B), HDL (C), and GS (D) between the three groups. A: the BNP level was the highest in the NA group and the lowest in the MVA group. B: HR was the highest in the NA group and lowest in the CAD group. C: the HDL level was the lowest in the CAD group and the highest in the NA group. D: GS was the highest in the MVA group and lowest in the CAD group. BNP, brain natriuretic peptide; HR, heart rate; HDL, high-density lipoprotein; GS, global strain; NA, non-angina; MVA, microvascular angina; CAD, coronary artery disease.

characteristics of CAD among patients with stable chest pain who had no evidence of other myocardial ischemia and only had cTnI elevation inappropriate for AMI who had undergone CAG, to confirm the necessity of CAG in patients with low to intermediate risk. According to our study, more than half of the patients (59%) were diagnosed with CAD and, most patients underwent PCI or CABG (74%), and two patients were diagnosed with VA using the ergonovine provocative test. A recent study from the DISARCHGE Trial group [35] that compared computed tomography (CT) or invasive CAG in patients with stable chest pain and intermediate pre-test probability of CAD showed similar detection rates of CAD and treatment strategy (PCI or CABG), and also showed a similar rate of occurrence of major adverse cardiovascular events in the CT or CAG groups. They explained that the lower rate of major adverse cardiovascular events in the CAG groups was possibly due to improvements in the methods used to perform CAG and general improvements in cardiovascular care (Maurovich-Horvat P et al., 2018).

According to the results of this study, more than half of the patients were diagnosed with CAD, and most of them received PCI, suggesting that it is reasonable to perform CAG in patients with stable chest pain and cTnI elevation only, which is considered to have low to intermediate pre-test probabilities. In particular, patients with DM, low HDL, or subclinical myocardial dysfunction, such as an increase in RWT or decrease in E′ velocity in TTE, were more likely to have CAD. Silent myocardial ischemia, atypical chest pain, and stable chest pain are very common in patients with DM [36], therefore, even if other diagnostic tests (ECG or TTE) do not show any specific findings, if cTnI is elevated, performing a test to exclude CAD (such as CAG) is considered useful. Among these parameters, a low HDL level was independently associated with the presence of CAD in our study.

In this study, although a small number of patients were enrolled, sub-analysis was performed by dividing patients without CAD into MVA and NA groups according to their clinical symptoms and response to anti-anginal medications. Interestingly, patients with CAD and MVA had some common characteristics, whereas patients with MVA and NA had distinct characteristics. As shown in Fig. 1, DM had the highest prevalence in the order of CAD, MVA, and NA, and current alcohol drinkers had the highest prevalence in the MVA group. As shown in Fig. 2, NA patients showed the highest BNP level and HR, as well as the highest HDL level. Considering the diagnosis of NA (asthma or COPD exacerbation, severe GERD, hyponatremia, infection, and others), the possibility of CAD due to atherosclerosis is low, and it is considered that a subtle elevation of cardiac troponin is accompanied by a systemic disease that places a

burden on the heart [15,16]. Patients with NA showed the highest BNP level and HR in our study. There are several debates regarding the correlation between alcohol and angina, but it is assumed that excessive alcohol consumption may induce endothelial dysfunction and inhibition of angiogenesis, which induces myocardial dysfunction and inflammation, leading to coronary microvascular circulation dysfunction and angina [28]. A recent cohort study found that even after adjustment for a healthy lifestyle, if you refer to the results of a recent cohort study that not only excessive drinking intake, but also drinking alcohol is associated with cardiovascular disease [37]. Referring to the results of this study, although our study did not investigate the amount of drinking, it may be a significant finding that drinking is associated with MVA. In addition, the fact that the proportion of drinking was higher in MVA patients than in CAOD patients suggests that patients with moderate drinking maintained a slightly healthier lifestyle, preventing conventional risk factors associated with CAOD. Interestingly, despite alcohol consumption being more prevalent in patients with MVA than in those with CAD, MVA patients showed the most favorable LV diastolic and systolic parameters (although we included patients with normal LV function, excluding preexisting cardiomyopathy, heart failure, and RWMA). It is impossible to conclude that alcohol consumption is associated with MVA but not CAD in our study because of the small sample size and lack of long-term follow-up data; however, further investigation may be required to investigate this relationship.

5. Clinical implications

This study showed a relatively high prevalence of stable CAD in patients with chest pain and elevated cardiac TnI only, without elevation of CK-MB, ST change on ECG, or RWMA on echocardiography, especially in those with chest pain and other risk factors (DM, low HDL et al.). In addition, 40% of patients were clinically diagnosed with MVA among those without CAD (no obstruction detected by CAG). These patients had slightly different clinical aspects compared with those of patients with CAD and NA. Patients with NA showed non-cardiac causes of elevated troponin levels, such as asthma or COPD exacerbation, severe GERD, hyponatremia, and infection (data not shown).

5.1. Limitations

This study has several limitations. First, this was a single-center study with a small sample size. Second, since not all patients had undergone tests such as the Holter or telemetry tests, the diagnosis of atrial fibrillation (AF) or other arrhythmias that can cause chest pain or cTnI elevation may have been missed. Third, this was a cross-sectional study and we did not assess the long-term prognosis of patients with elevated cardiac troponin levels. However, this is the first study to investigate the prevalence of CAD and its related factors in patients diagnosed with stable CAD and chest pain, and to compare clinical and other factors between patients with and without CAD. We believe that these findings might help improve diagnosis of stable CAD in patients with chest pain and elevated cTnI levels.

6. Conclusion

In conclusion, our findings highlight that elevated cTnI alone is needed to perform CAG in patients with chest pain. Low HDL levels were independently associated with stable CAD in patients with chest pain and elevated cTnI levels. In the subgroup analysis, CAD was associated with DM and low HDL, and MVA was associated with alcohol consumption and more favorable echocardiographic parameters.

Ethics committee approval

This study was approved by the Institutional Review Board (IRB no. 2022-11-023).

Informed consent

Informed consent was not obtained from all individual participants included in the study, because this study was a retrospective, observational study and was analyzed through medical record review. There was no information the authors had access to potentially identifying patient information. The need for informed consent was waived by the ethics committee.

Declaration of interests

The authors have no conflicts of interest to declare.

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