MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2019; 25: 6034-6042
DOI: 10.12659/MSM.913891

Received: 2018.10.31
Accepted: 2019.03.18
Published: 2019.08.13

Increased Ratio of Circulating T-Helper 1 to T-Helper 2 Cells and Severity of Coronary Artery Disease in Patients with Acute Myocardial Infarction: A Prospective Observational Study

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

B Chang Li
CD Wenxia Zong
E Ming Zhang
E Yanming Tu
F Qiyu Zhou
D Mingke Ni
A Zhiyong Li
AE Haizhen Liu
ACE Jingyi Zhang

Hubei No. 3 People's Hospital of Jianghan University, Wuhan, Hubei, P.R. China

Corresponding Author: Jingyi Zhang, e-mail: jingyi_zhang123@sina.cn
Source of support: Departmental sources

Background: This study aimed to determine the association between CD4-positive T-helper (Th) cell subsets, T-helper 1 (Th1) and T-helper 2 (Th2) in patients with acute myocardial infarction (AMI) and the severity of coronary artery disease (CAD) determined by coronary artery angiography.

Material/Methods: Three groups of patients with AMI who underwent coronary angiography and percutaneous coronary intervention (PCI) included patients with stable CAD (n=35), ST-segment elevation myocardial infarction (STEMI) (n=30), and non-STEMI (NSTEMI) (n=35), and controls (n=33). Measurement of high-sensitivity cardiac troponin T (hs-cTnT) was performed. The numbers of circulating CD4-positive Th1 and Th2 cells were measured using flow cytometry. Plasma levels of interferon-γ (IFN-γ) and interleukin-4 (IL-4) were measured using enzyme-linked immunosorbent assay (ELISA).

Results: An increase in the Th1 lymphocyte population was associated with more CAD, and an increased Th1/Th2 ratio was found in patients with NSTEMI and STEMI (controls 7.27±2.98; stable CAD 7.58±2.52; NSTEMI 16.62±2.74; and STEMI 22.32±7.35) (P<0.001). The proportion of Th1 cells and the Th1/Th2 ratio increased as the number of affected arteries, the degree of stenosis, and the lesion length increased. At a median follow-up of 18.2 months, patients with CAD and an increased Th1/Th2 ratio had a significant increase in adverse cardiac events compared with patients with a reduced Th1/Th2 ratio (log-rank, P=0.042).

Conclusions: An increased ratio of circulating Th1 to Th2 cells in patients with AMI was associated with the severity of CAD determined by angiography.

MeSH Keywords: Adaptive Immunity • Atherosclerosis • Interleukin-1 • Myocardial Infarction

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/913891

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Background

Worldwide, acute myocardial infarction (AMI) due to coronary artery disease (CAD) is a leading cause of morbidity and mortality [1,2]. Chronic inflammation and the cellular immune response are associated with stable and unstable CAD and with AMI [3–5]. AMI is characterized by local inflammation in the myocardium, and plaque rupture of the coronary artery atherosclerotic plaque is associated with thrombosis and coronary artery occlusion [5–8].

Recent studies have shown that T-lymphocytes in human peripheral blood are heterogeneous. T-lymphocytes can be typed according to the expression patterns of cell surface proteins, intracellular proteins, and function, including the release of cytokines and their capacity to recruit B-lymphocytes and macrophages [9]. CD3 expression is associated with T-lymphocytes and can distinguish them from B-lymphocytes. CD4-positive T-lymphocytes, or T helper cells, recognize and present antigens through the major histocompatibility complex (MHC) class I or II molecules.

Preclinical studies have shown that a deficiency of CD4-positive T-cells in Apoe–/– mice inhibits the development of intimal arterial lesions, but the effect of CD8-positive T-cells remains unclear from mouse model studies [10,11]. In a mouse model that studied CD4-positive T-cell subsets, depletion of T helper 1 (Th1) subsets associated with deficiency of T-bet, a Th1-specific T box transcription factor, reduced interferon-γ (IFN-γ) signaling and murine intimal atheroma [12]. However, the role of Th2 subsets in human atherosclerosis remains poorly understood, and the findings have been controversial. In clinical studies, cytokine levels including interleukin-2 (IL-2) and IFN-γ are significantly increased in patients with acute coronary syndrome (ACS) compared with patients with stable CAD, indicating that increased activation of Th1 lymphocytes may contribute to plaque instability [1314]. However, the levels of cytokines associated with Th2 cells showed no differences between patients with ACS and patients with stable CAD [15,16].

Therefore, this study aimed to determine the association between CD4-positive T-helper cell subsets, Th1 and Th2, in patients with AMI and the severity of CAD determined by coronary artery angiography.

Material and Methods

Study population

This study was approved by the Research Ethics Committees of the Third Peoples' Hospital of Hubei Province. Written informed consent was provided by all study participants. This was a prospective observational study that enrolled three groups of patients from December 2017 to July 2018 in a single center. Patients were recruited who had a diagnosis of acute myocardial infarction (AMI) who underwent coronary artery angiography and who were treated with percutaneous coronary intervention (PCI). Three study groups included the AMI group that included 30 patients who were diagnosed with ST-segment elevation myocardial infarction (STEMI); 35 patients were diagnosed with non-ST-segment elevation myocardial infarction (NSTEMI); and 35 patients were diagnosed with stable coronary artery disease (CAD), confirmed by coronary angiography. Thirty-three subjects were included in the control group who were asymptomatic with no history of AMI and with a history of coronary artery angiography without coronary artery narrowing ≥50%.

Study inclusion and exclusion criteria

Before PCI, all patients were given a loading dose of 300 mg of clopidogrel and 300 mg of aspirin as antiplatelet therapy, and 3000 U of intravenous heparin before coronary angiography, and were then given supplemental heparin at a dose of 70–100 U/kg, with a maximum dose of 8000 U. The study inclusion criteria were based on the diagnosis of STEMI and the coronary angiography findings. Patients with STEMI were diagnosed with symptoms of acute ischemic chest pain, and dynamic changes in the electrocardiogram (ECG) that included ST-segment elevation of at least 1 mm (0.1 mV) in the limb leads and at least a 2 mm elevation in the precordial leads. Myocardial infarction was also confirmed by measurement of high-sensitivity cardiac troponin T (hs-cTnT). The coronary angiography results indicated that at least one of the coronary arteries was totally occluded. Patients were excluded from the study who had a previous history of myocardial infarction, coronary revascularization, congestive heart failure, cardiomyopathy, pericardial disease, peripheral vascular disease, hematologic disease, cancer, inflammatory disease, congenital diseases, and liver or renal disease.

Quantitative assessment of CAD by coronary artery angiography

Quantitative assessment of CAD was performed using coronary angiography, as previously described [17]. A semiquantitative evaluation of the coronary artery burden of atheromatous plaque from the invasive coronary angiography (ICA) images was performed by an interventional cardiologist. A minimum of six projections of the left and right coronary systems were acquired in each patient. The assessment of segments of the atherosclerotic plaques was based on the 18-segment classification system from the Society of Cardiovascular Computed Tomography (SCCT) [18]. Briefly, significant CAD was defined as the presence of coronary artery luminal diameter narrowing

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≥50% in the left anterior descending (LAD) coronary artery, left circumflex coronary artery, right coronary artery, and their main branches. Stenosis of the main trunk of the left coronary artery was considered as two-vessel disease. The burden of atherosclerotic plaques was evaluated by the length of the intimal plaque (>20 mm were long lesions), the degree of coronary artery stenosis with and without calcification was classified as moderate (50–69%), severe (70–99%), or occluded (100%), and the number of coronary vessels with significant stenosis was evaluated. In cases with multivessel disease, the highest degree of stenosis was identified for further investigation.

Flow cytometry for T helper (Th) cell subsets

Approximately 5 ml of peripheral blood samples were taken on the day after hospital admission from the control group, patients with stable CAD, and patients with STEMI and NSTEMI who had fasted overnight. All peripheral blood samples from the study population were obtained before coronary angiography and PCI. T-lymphocyte subsets were analyzed in a whole-blood assay using 100 µl of whole blood. Forward scatter (FSC) and side scatter (SSC) gating was used to exclude cell debris. Anti-human antibodies were conjugated to different fluorochromes for flow cytometry. T-lymphocytes were identified and gated using a phycoerythrin (PE)-conjugated antibody to CD3 (UCHL1) (BD Biosciences, Franklin Lakes, NJ, USA) for the dot plots. Whole blood cells were stained with an antibody to CD4 conjugated to PerCP-Cy5.5 (clone SK3) (BD Biosciences, Franklin Lakes, NJ, USA), an antibody to IFN-γ conjugated to fluorescein isothiocyanate (FITC) (clone B27) (BD Biosciences, Franklin Lakes, NJ, USA), and an antibody to IL-4 APC (clone MP4-25D2) (BD Biosciences, Franklin Lakes, NJ, USA). Antibodies were incubated with the cells for 15 min at room temperature and analyzed using a Cell Lab Quanta SC Flow Cytometer (Beckman Coulter, Brea, CA, USA). The flow cytometry for identifying T-lymphocyte subsets was performed by one expert technician who was unaware of the patient groups and their coronary angiography findings.

Measurements of plasma cytokine levels

The plasma levels of IL-4 and IFN-γ were measured by commercial enzyme-linked immunosorbent assay (ELISA) kits for human IL-4 (Thermofisher Scientific, Waltham, MA, USA) and human IFN-γ (R&D Systems, Minneapolis, MN, USA). ELISA was performed according to the manufacturer's protocols. The absorbance of the plates was measured at 570 nm using a microplate reader and converted to plasma concentrations for IL-4 and IFN-γ.

Follow-up assessment

Follow-up data were obtained by phone calls conducted between January 2019 and March 2019 by an independent investigator. The endpoints evaluated included incidents of cardiac death, nonfatal MI, and coronary revascularization. Cardiac death was defined as death caused by MI, ventricular arrhythmia or cardiogenic shock. Coronary revascularization was defined as the requirement for PCI of the affected vessels or a requirement for coronary artery bypass grafting. A composite endpoint was constructed from all three endpoints for analysis.

Statistical analysis

Statistical analysis was performed using SPSS version 20.0 (IBM, Chicago, IL, USA). Data were reported as the mean ± standard deviation (SD) for continuous variables and as proportions or percentages for categorical variables. Analysis of variance (ANOVA) and the Bonferroni correction were performed to compare the differences between the controls, patients with stable CAD, patients with NSTEMI, and patients with STEMI. The differences between categorical variables were determined using the chi-squared (χ^2) test. Event rates were estimated with Kaplan-Meier curves and compared with a log-rank test. Two-sided statistical analysis was performed. A P-value <0.05 was considered statistically significant.

Results

T-helper (Th) cell subsets, T-helper 1 (Th1) and T-helper 2 (Th2), in patients with acute myocardial infarction (AMI)

The baseline characteristics of the patients included in the study are shown in Table 1. Peripheral blood samples were collected and sorted by flow cytometry to analyze the two distinct T-lymphocyte subsets (Th1 and Th2). The Th1 subset was defined as CD4-positive T-lymphocytes expressing IFN-γ but not IL-4. The Th2 subset was defined as CD4-positive T-lymphocytes expressing IL-4 but not IFN-γ. As shown in Table 2, compared with controls and patients with stable coronary artery disease (CAD), the percent of neutrophils and the neutrophil to lymphocyte ratio were significantly increased in patients with ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI). Although the percentage of Th2 subsets in the total CD3-positive T-lymphocyte population were not significantly different between the four study groups, the percentage of Th1 subsets in total CD3-positive T-lymphocytes and Th1/Th2 ratio were significantly increased in patients with AMI when compared with controls and patients with stable CAD (Table 2).

A post hoc Bonferroni correction was used to further correct and validate the differences in the percentage of Th1 subsets and Th1/Th2 ratio between patients with stable CAD and patients with NSTEMI and between patients with stable CAD and patients with STEMI (Figure 1A, 1B).

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Table 1. Baseline characteristics of the four study groups.

	Control (n=33)	SCAD (n=35)	NSTEMI (n=35)	STEMI (n=30)	p-Value
Age, yrs	66.4±10.8	65.8±9.4	63.7±9.0	68.1±11.4	0.373
Male	19 (57.6)	17 (48.6)	18 (51.4)	20 (66.7)	0.478
Smoking	11 (33.3)	10 (28.6)	14 (40.0)	16 (53.3)	0.199
Diabetes	7 (21.2)	10 (28.6)	10 (28.6)	9 (30.0)	0.853
Fasting glucose, mmol/L	5.9±2.1	6.9±1.9	6.5±1.8	7.4±3.2	0.066
Hypertension	8 (24.2)	18 (51.4)	21 (60.0)	20 (66.6)	**0.004**
Triglyceride, mmol/L	1.7±1.2	1.8±1.5	1.7±1.5	2.0±1.7	0.836
Cholesterol, mmol/L	4.5±1.4	4.6±1.6	4.8±1.7	5.0±1.6	0.601
LDL-C, mmol/L	2.7±1.2	2.9±1.3	2.8±0.7	3.1±1.2	0.537
HDL-C, mmol/L	1.0±0.3	1.1±0.4	1.0±0.2	1.2±0.4	0.114
BUN, mmol/L	5.8±1.5	5.8±2.0	5.9±1.3	6.2±2.1	0.778
Creatinine, mg/L	77.9±31.0	80.4±27.5	79.8±19.4	82.0±23.1	0.937
hs-CRP, mg/L	1.01±0.32	1.03±0.28	1.49±0.43	1.89±0.28	**<0.001**
hs-cTnT, μg/L	0.01±0.01	0.02±0.01	0.09±0.04	0.84±0.23	**<0.001**
CK-MB, ng/ml	31.5±10.2	41.8±10.8	64.2±11.8	92.7±41.0	**<0.001**
Coronary angiography					
Long lesions	–	12 (34.3)	19 (54.3)	16 (53.3)	
Affected vessels					0.21
1-vessel	–	18 (51.4)	10 (28.6)	15 (50.0)	
2-vessel	–	12 (34.3)	17 (48.6)	10 (33.3)	
≥3-vessel	–	5 (14.3)	8 (22.9)	5 (16.7)	
Stenosis					**<0.001**
Moderate	–	27	8	0	
Severe	–	8	23	5	
Occlusion	–	0	4	25	

SCAD – stable coronary artery disease; STEMI – ST-segment elevation myocardial infarction; NSTEMI – non-STEMI; LDL – low-density lipoprotein; HDL – high-density lipoprotein; BUN – blood urea nitrogen; CRP – C-reactive protein; CK-MB – creatine kinase-muscle/brain; hs-TnT – high-sensitivity cardiac troponin T.

Table 2. Total counts and proportions of peripheral blood cells in each group.

	Control (n=33)	SCAD (n=35)	NSTEMI (n=35)	STEMI (n=30)	p-Value
WBC, $\times 10^9$/ml	6.53±1.64	6.83±1.82	6.89±1.87	7.24±2.05	0.506
Neu, % WBC	59.37±8.25	60.04±7.85	68.82±9.04	77.63±9.48	**<0.001**
Lym, % WBC	29.48±7.84	28.15±6.46	26.82±6.83	19.18±5.24	**<0.001**
Neu/Lym ratio	2.02±0.88	2.13±0.91	2.57±0.94	4.03±1.03	**<0.001**
Th1, % CD3+ T-cells	6.74±2.18	6.90±2.07	12.47±2.73	15.18±3.68	**<0.001**
Th2, % CD3+ T-cells	0.94±0.73	0.91±0.82	0.75±0.63	0.68±0.50	0.362
Th1/Th2 ratio	7.27±2.98	7.58±2.52	16.62±2.74	22.32±7.35	**<0.001**

Values are mean ±SD. SCAD – stable coronary artery disease; STEMI – ST-segment elevation myocardial infarction; NSTEMI – non-ST-segment elevation myocardial infarction; DC – dendritic cell; Lym – lymphocyte; mDC – myeloid dendritic cell; Mon – monocyte; pDC – plasmacytoid dendritic cell; PMNs – polymorphonuclear neutrophils.

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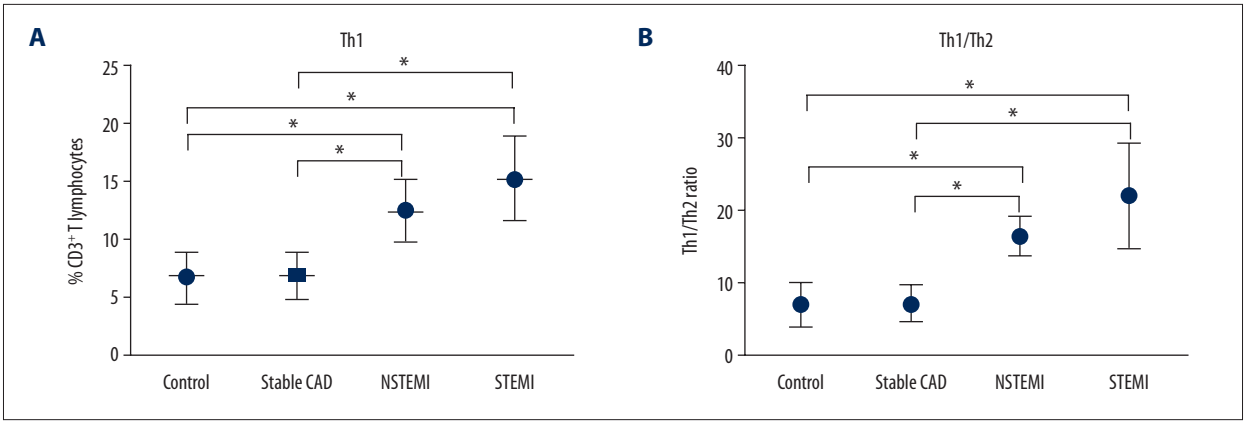

Figure 1. Comparison of CD4-positive Th1 cells and the Th1/Th2 ratio in the four study groups. (**A**) Comparison of CD4-positive Th1 cells between the four groups. (**B**) Comparison of the Th1/Th2 ratios in the four study groups. CAD – coronary artery disease; NSTEMI – non-ST-segment elevation myocardial infarction; STEMI – ST-segment elevation myocardial infarction; Th1 – T helper 1 subset; Th2 – T helper 2 subset. * P<0.05.

The association of Th subsets with the severity of CAD was measured by coronary angiography and showed that there was a gradual increase in the percentage of Th1 subsets in the total population of CD3-positive T-lymphocytes and Th1/Th2 ratio with an increase in the number of affected vessels, the degree of coronary artery stenosis, and the length of the coronary artery lesion (Figure 2A–2I).

Plasma levels of IFN-γ were significantly increased in patients with AMI compared with controls and patients with stable CAD

IFN-γ is a pro-inflammatory cytokine released from Th1 lymphocytes. Enzyme-linked immunosorbent assay (ELISA) showed that plasma levels of IFN-γ in patients with STEMI and NSTEMI were significantly increased when compared with patients with stable CAD and controls (control 2.15±0.73 pg/ml; stable CAD 2.37±0.82 pg/ml; NSTEMI 6.83±1.24 pg/ml; STEMI 7.92±1.30 pg/ml) (P<0.001) (Figure 3A). In patients with NSTEMI and STEMI, plasma levels of IFN-γ were significantly associated with plasma levels of high-sensitivity cardiac troponin T (hs-cTnT) (r=0.833; P<0.001) (Figure 3B). These data suggest that plasma IFN-γ was not only increased in patients with AMI but was also associated with the severity of AMI, which was consistent with the findings of Th2 subsets in patients with AMI. However, there was no significant difference in plasma levels of IL-4 between the controls and patients with stable CAD and AMI (control 100.6±27.4 ng/ml; stable CAD 124.8±31.5 ng/ml; NSTEMI 115.3±30.8 ng/ml; STEMI 129.6±35.4 ng/ml) (P=0.57) (Figure 3C).

An increased Th1/Th2 ratio was associated with adverse cardiac events

Follow-up was completed for all patients included in the study, with a median follow-up time of 18.2 months. A total of 12 adverse cardiac events occurred during the follow-up period and included two cardiac deaths, seven non-fatal cases of AMI, and five cases of coronary revascularization. With the median Th1/Th2 ratio of 15, the patients were divided into two groups to evaluate the predictive value of the Th1/Th2 ratio for adverse cardiac events. Within the follow-up period, only four adverse cardiac events were identified that included three cases of non-fatal MI and two coronary revascularization events, which occurred in patients with a reduced Th1/Th2 ratio, corresponding to an overall event-free survival rate of 92.5%. The majority of adverse cardiac events occurred in patients with a high Th1/Th2 ratio (n=10) with an overall event-free survival rate of 78.7%. Event-free survival curves for patients in both groups are shown in Figure 4 (log-rank, p=0.042).

Discussion

Atherosclerosis is a chronic inflammatory disease that is associated with a cell-mediated immune response that includes T-lymphocytes and macrophages [8]. In the early stage of atherosclerosis, oxidized low-density lipoprotein (LDL) provokes an inflammatory response with the recruitment of circulating immune cells that include lymphocytes and monocytes into lipid-rich vulnerable plaques [19,20]. T-cells are present at all stages of atherosclerosis [5,7]. Given the advances in immune technologies and the feasibility of genetic manipulation in animal models of atherosclerosis, an increasing number of studies have identified some important immune mechanisms during atherosclerosis and myocardial infarction. The role of CD8-positive T-cells in atherosclerosis and myocardial infarction remained controversial, and CD8-positive T-cells are less frequently found in atherosclerotic plaques and myocardial infarction and deficiency in CD4-positive T-cells contribute to the compensatory changes in the CD8-positive T-cell population.

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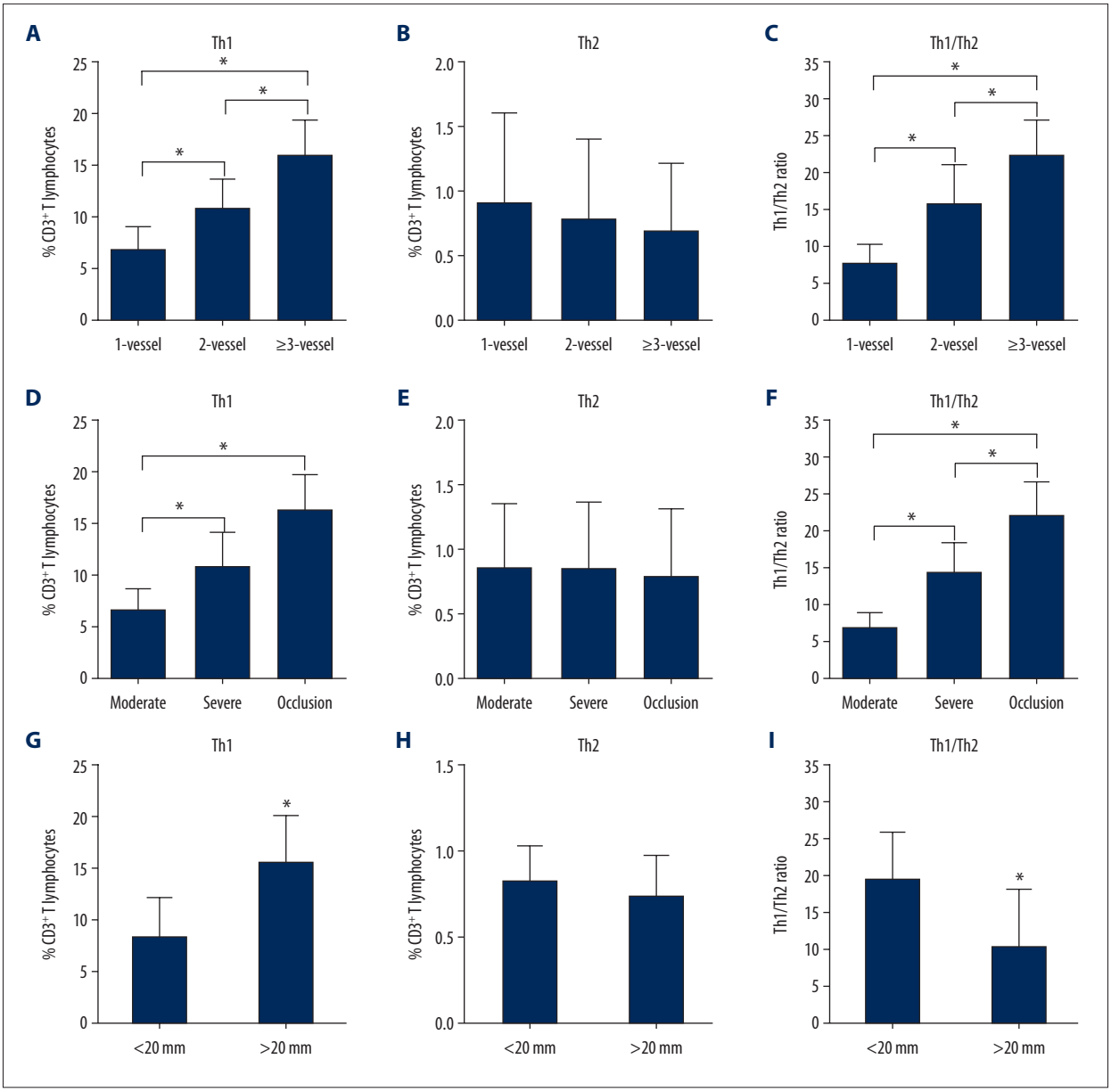

Figure 2. Changes in CD4-positive Th1 cells and Th2 cells in the four study groups. (**A–C**) Comparison of CD4-positive Th1 cells and Th2 cells according to the number of affected vessels. (**D, E**) Comparison of CD4-positive Th1 cells and Th2 cells according to the degree of coronary artery stenosis. (**F–I**) Comparison of CD4-positive Th1 cells and Th2 cells according to the lengths of the coronary artery lengths. CAD – coronary artery disease; NSTEMI – non-ST-segment elevation myocardial infarction; STEMI – ST-segment elevation myocardial infarction; Th1 – T helper 1 subset; Th2 – T helper 2 subset. * P<0.05.

CD4-positive T-helper (Th) cell consist of several distinct subpopulations, which have different roles and can differentiate in response to antigen-presenting cells and various extracellular inflammatory stimuli [21]. CD4-positive T-cells account for approximate 70% of resident T-cells in atherosclerotic plaques [20,22]. Zhou et al. [23] found that depletion of CD4-positive T-cells in Apoe-/- mice caused the reduction in the burden of atherosclerotic plaques. Reduction in CD4-positive T-cells is associated with myocardial remodeling and increased ventricular rupture, and CD4-positive T-helper 1 (Th1) subsets are the major components of CD4-positive T-cells in the vessel wall and myocardium [24].

Atherosclerotic plaque rupture is the main cause of acute coronary syndrome (ACS), and a change in the proportion of the Th1 subset in peripheral blood has been shown to promote plaque rupture in Apoe–/– mice, which may drive ACS [24]. In contrast to CD4-positive Th1 subsets, current studies on CD4-positive

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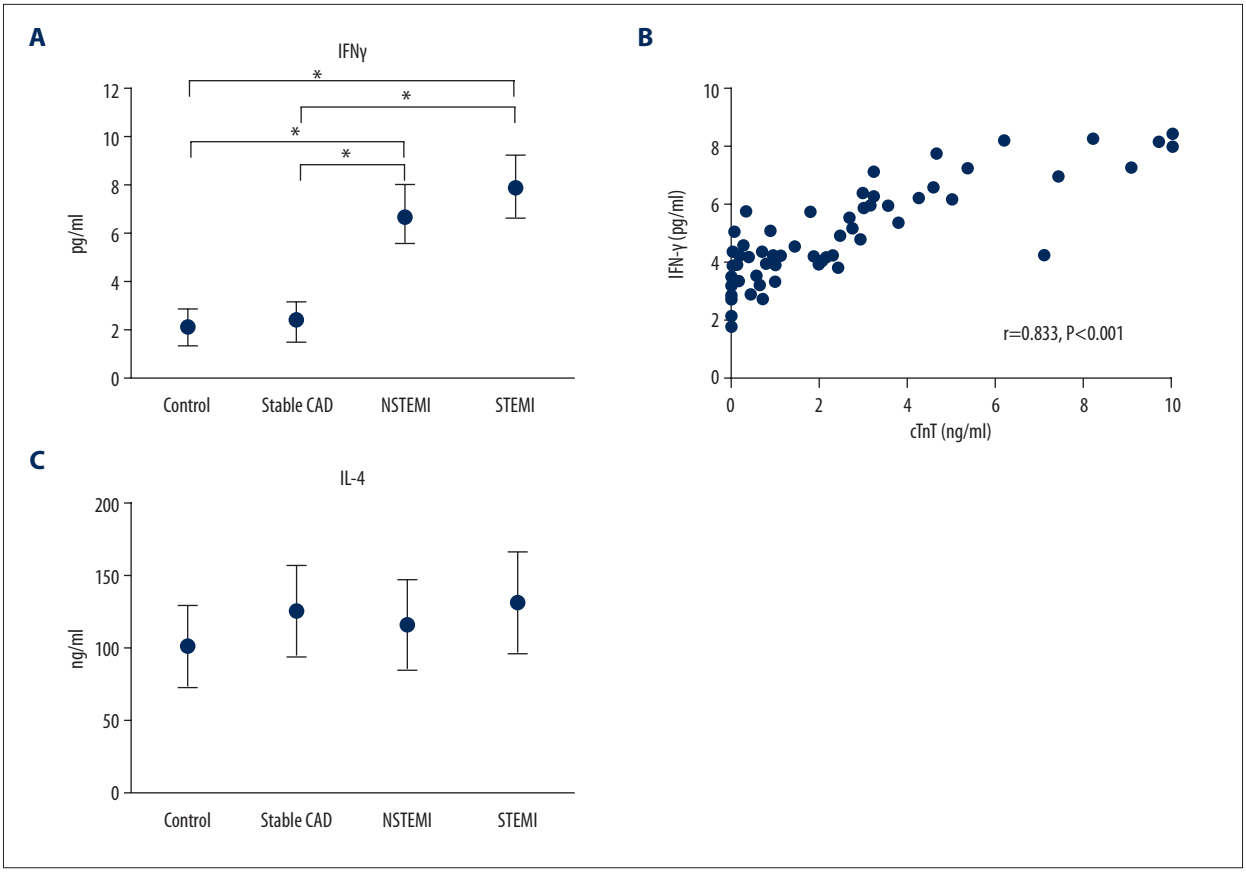

Figure 3. Comparison of plasma IFN-γ and IL-4 levels in the four study groups. (**A**) Comparison of plasma IFN-γ levels between the four groups. (**B**) Correlation of IFN-γ with high-sensitivity cardiac troponin T (hs-cTnT) in patients with NSTEMI and STEMI. (**C**) Comparison of plasma IL-4 levels between the four groups. CAD – coronary artery disease; NSTEMI – non-ST-segment elevation myocardial infarction; STEMI – ST-segment elevation myocardial infarction; Th1 – T helper 1 subset; Th2 – T helper 2 subset; hs-cTnT – high-sensitivity cardiac troponin T; IFN-γ – interferon-γ; IL-4 – interleukin-4. * P<0.05.

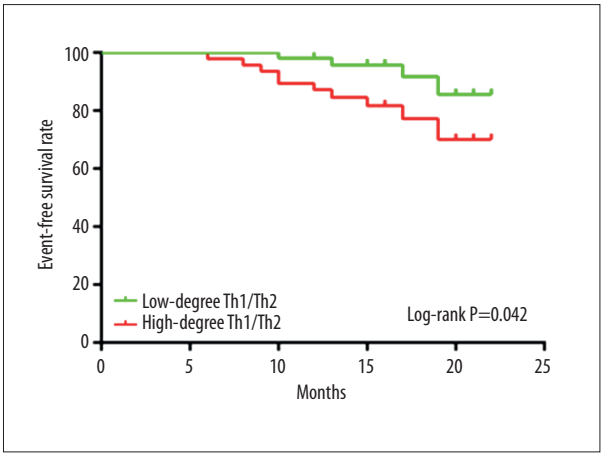

Figure 4. Event-free survival for the composite endpoint of all-cause mortality, non-fatal myocardial infarction, and coronary revascularization, according to the Th1/Th2 ratio.

T-helper 2 (Th2) subsets remain controversial [25]. Knockout of IL-4 in LDLR–/– mice fed a high-fat diet showed a reduced plaque burden and implied a pro-atherogenic effect of CD4-positive Th2 subsets [26]. Consistent with this finding, in the present study, circulating CD4-positive Th1 subsets represented an increased proportion of the peripheral blood CD4-positive T-lymphocytes. Also, a significantly increased percentage of CD4-positive Th1 subsets, and an increased Th1/Th2 ratio was observed in patients with NSTEMI and patients with STEMI compared with patients with stable CAD and controls, and no differences were found between the four groups. Yan et al. [4] showed increased mRNA expression of Th1-associated cytokines and reduced mRNA expression of Th2-associated cytokines in patients with AMI when compared with controls, reflecting a shift towards Th1 dominance in myocardial infarction.

Also, the findings of the present study showed a significant correlation between the proportion of CD4-positive Th1 subsets and the Th1/Th2 ratio, the number of affected coronary arteries, the degree of coronary artery stenosis, and the lesion

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length, which indicated that an increased Th1/Th2 ratio might be associated the severity of atherosclerosis. Although several previously published studies have evaluated the prognostic value of circulating innate immune cells in patients with CAD, there remains a need for further research to determine the clinical predictive value of evaluating circulating immune cells [27]. The findings from the present study showed that patients with CAD who had an increased Th1/Th2 ratio had an increased incidence of adverse cardiac events when compared with patients with a low Th1/Th2 ratio, suggesting the possible positive predictive value of the Th1/Th2 ratio for cardiac clinical events.

In previous studies, the cytokines IFN-γ, IL-4, and IL-17α have been shown to be associated with the differentiation of CD4-positive T helper cells into their subsets in the myocardium following AMI [7,19,28]. CD4-positive Th1 subsets retain cellular immunity mainly by secreting IL-1, IL-2, IL-12, and IFN-γ, while CD4-positive Th1 subsets secrete IL-4, IL-6, and IL-25 to activate B-lymphocytes and generate antibodies. In line with the findings of circulating CD4-positive Th1 and Th2 subpopulations in the present study, plasma levels of IFN-γ were significantly increased in patients with STEMI and NSTEMI compared with patients with stable CAD and controls, while there was no difference in plasma levels of IL-4 between the four study groups. Szodoray et al. [29] measured the circulating levels of cytokines associated with the differentiation and function of CD4-positive Th1 and Th2 subpopulations and showed that levels of IL-1 that is specific for CD4-positive Th1 subsets were significantly increased in patients with ACS and the Th1/Th2 ratio shifted towards a Th1 predominance [25,30,31]. However, in a previous study, levels of IFN-γ and IL-4 were not significantly correlated with the severity of CAD assessed by the Gensini score for the expression of coronary angiography findings [30]. These conflicting data could be attributed to the fact that the Gensini score was evaluated by different physicians in this previous study [30]. Because the present study was a cross-section observational study, it was not possible to propose a causal link between a change in the Th1/Th2 ratio and the incidence of ACS, and the association between with peripheral Th1 and Th2 cells and the risk for ACS requires further investigation by prospective controlled clinical studies.

Conclusions

In patients with acute myocardial infarction (AMI), the severity of angiographically evaluated coronary artery disease (CAD) was associated with an increased ratio of CD4-positive T-helper (Th) cell subsets, T-helper 1 (Th1) and T-helper 2 (Th2).

Conflict of interest

None.

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