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Diagnostic role of echocardiography in patients admitted to the emergency room with suspect no-ST-segment elevation acute myocardial infarction

L. MANFREDONIA, G.A. LANZA, F. CRUDO, P. LAMENDOLA, F. GRAZIANI, A. VILLANO, G. LOCOROTONDO, V. MELITA, E. MENCARELLI, F. PENNESTRÌ, A. LOMBARDO, A. DE VITA, S.E. RAVENNA, A. BISIGNANI, F. CREA

Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Institute of Cardiology, Rome, Italy.

Abstract. – OBJECTIVE: We investigated whether echocardiography may help identify, among patients admitted with a suspect of non-ST-segment elevation acute myocardial infarction (NSTEMI), those with athero-thrombotic coronary artery disease (CAD).

PATIENTS AND METHODS: We studied consecutive patients admitted with a clinical suspect of first NSTEMI. Echocardiography was assessed within 24 hours from admission. Patients were divided into two groups, according to the results of coronary angiography: 1) patients with obstructive stenosis (≥ 50%) and/or images of thrombosis in one or more coronary arteries (CAD group); 2) patients with no evidence of obstructive coronary arteries (NOCAD group).

RESULTS: Of 101 patients enrolled in the study, 53 (52.5%) showed obstructive CAD and 48 (47.5%) NOCAD. At echocardiographic examination, regional wall motion abnormalities were found in 52.8% of patients in the CAD group and 43.7% in the NOCAD group (p=0.43). Left ventricle ejection fraction was 56.4±6.8 *vs.* 54.7±9.8% (p=0.30) and wall motion score index was 1.16±0.26 *vs.* 1.21±0.32 (p=0.39) in the two groups, respectively. A multivariable logistic regression independent predictors of obstructive CAD included age, male gender, typical angina, diabetes and hypertension.

CONCLUSIONS: Our data showed that, in patients with acute chest pain and increased serum troponin T concentration, routine standard echocardiography does not significantly improve the diagnostic accuracy for the presence of obstructive CAD.

Key Words

Echocardiography, Troponin, Non-ST-segment elevation acute myocardial infarction.

Introduction

Among patients admitted to an emergency room because of acute chest pain suspect of acute coronary syndrome, the diagnosis of acute myocardial infarction is now mainly achieved through the detection of rise and fall of serum troponin levels, with or without ischemic changes at the electrocardiogram (ECG), based on the assumption that troponin elevation is highly specific of ischemic myocardial cell necrosis[1-4].

However, numerous studies[5] have shown that an increase in serum troponin levels may result from non-ischemic myocardial cell damage. Accordingly, among patients with a suspect of no-ST-segment elevation acute myocardial infarction (NSTEMI), mainly based on troponin elevation, about 5-15% are found to have coronary arteries free of significant athero-thrombotic disease[6-8]. Echocardiography is the reference imaging test for the detection of global and regional left ventricle wall motion abnormalities (LVWMA) and, therefore, it might be helpful identify, among patients with acute chest pain and troponin elevation, those with classical NSTEMI. Indeed, echocardiography is recommended by international guidelines to support the diagnosis of NSTEMI by possibly detecting new regional LVWMA[3,4]. However, the diagnostic role of standard echocardiography in this context is not well defined. Thus, in this work, we aimed at assessing whether performing routine echocardiography in patients admitted for a suspected NSTEMI improves the diagnostic accuracy for the presence of significant obstructive athero-thrombotic coronary artery disease (CAD).

Corresponding Author: Gaetano A. Lanza, MD; e-mail: gaetanoantonio.lanza@unicatt.it

Patients and Methods

Patients

We prospectively enrolled consecutive patients admitted to the Emergency Department of our hospital between September 2016 and October 2017 with a suspect of NSTEMI, based on the presence of acute chest pain and increased serum troponin T level (i.e., above the maximal normal value for our laboratory) on admission, with or without significant ischemic abnormalities at ECG. Patients were excluded if they had: 1) any history of known CAD or other significant heart diseases (e.g., cardiomyopathy, moderate-to-severe valve disease); 2) ECG abnormalities (e.g., pacemaker rhythm, left bundle branch block, ventricular pre-excitation) that could interfere with the correct assessment of ischemic ECG changes and/or regional LVWMA.

Detailed clinical data were acquired for all patients, including cardiovascular risk factors and comorbidities. The study protocol was approved by the Institute's Committee on Human Research. Chest pain was considered typical if the patient referred an oppressive/constrictive retrosternal chest pain, with or without typical radiation (e.g., to the limbs, throat or jaw), not influenced by breathing, body position changes and finger pressure on the chest wall, whereas chest pain was considered atypical when presented characteristics different from any of these typical features.

Ischemic changes were considered to be present on admission standard ECG when ST-segment depression of 0.5 mm or more and/or T wave abnormalities were present.

Troponin T serum levels were measured every 6 hours in the first 24 hours and at 24-hour intervals thereafter, until discharge, using a high-sensitive chemiluminescence assay (Siemens ADVIA Centaur, Münich, Germany). When possible, usually due to the delay of coronary angiography beyond 12-24 hours from admission, we measured the time interval from the peak concentration of troponin T to the detection of troponin T levels lower than 20% and lower than 50% compared to the peak value. NT-pro-beta-type natriuretic peptide (NT-pro-BNP) was also measured on admission using a chemiluminescence method (Siemens Dimension Vista, Münich, Germany).

Echocardiography

Transthoracic mono-bi-dimensional color-Doppler echocardiography was performed as soon as possible, and in any case within 24 hours from admission and before coronary angiography, using a Toshiba Artida ultrasound machine (Tokyo, Japan) equipped with a 3.2 MHz transducer. All echocardiographic images were recorded on a workstation and analyzed separately off-line by two expert operators who were blinded to patient clinical and coronary angiographic data. Discordances were solved by consensus.

Global left ventricle systolic function was assessed by measuring left ventricle ejection fraction (LVEF) on 4-chamber and 2-chamber apical views using the modified Simpson method[8]. The assessment of regional LVWMA was made according to international recommendations[8]. The left ventricle was divided into 16 segments: anteroseptal, inferoseptal, inferior, inferolateral, anterolateral and anterior segments of the basal and midventricular portion of the left ventricle, and septal, inferior, lateral, and anterior segments of the apical portion of the ventricle. Each segment was analyzed in multiple views and scored according to the following scheme: 1 point for a normal or hyperkinetic segment; 2 points for a hypokinetic segment (reduced thickening); 3 points for an akinetic segment (absent or negligible thickening); 4 points for a dyskinetic segment (paradoxical systolic motion). Wall motion score index (WMSI) was calculated by averaging the scores of all left ventricle segments.

Coronary Angiography

Coronary angiography was performed within 72 hours from admission and could be completed by advanced intracoronary imaging study with ultrasound or optical coherence tomography at operator's discretion[9]. Based on invasive coronary results, patients were divided into two groups: 1) patients with significant coronary artery stenosis ($\geq$ 50%) and/or images demonstrating or supporting a recent thrombosis in at least one epicardial coronary segment (CAD group); 2) patients without any significant coronary artery stenosis (NOCAD) or suspect of recent thrombosis, in the presence of completely normal coronary arteries or coronary stenoses > 0% but < 50% of lumen diameter in one or more epicardial coronary vessels (NOCAD group).

Statistical Analysis

The normal distribution of variables was assessed by the Kolmogorov-Smirnov test. Between-group comparisons were made by independent *t*-test or Mann-Whitney U-test for continuous variables, as indicated. Categorical

variables were compared by Fisher exact test. Multivariable logistic regression was applied to identify the independent predictors of obstructive CAD; to this aim, only clinical and laboratory variables with $p \leq 0.1$ at standard statistical analyses were included in the multivariable model.

Data are presented as mean±SD or proportion, unless differently indicated. A p-value <0.05 was always considered for statistical significance. Data were analyzed using the SPSS 21.0 software system (SPSS Inc., Florence, Italy).

Results

Clinical and Angiographic Findings

The main clinical data of the two groups of patients are summarized in Table I. Overall, 101 patients were enrolled in the study, 53 of whom (52.5%) had athero-thrombotic CAD, whereas 48 (47.5%) showed NOCAD at angiography.

CAD patients were older, more often men, and showed higher body mass index and number of cardiovascular risk factors compared to NOCAD patients. Furthermore, a higher proportion of patients in the CAD group was taking cardiovascular or antidiabetic drugs and was classified as having typical ischemic chest pain (71.4 *vs.* 28.6 %, respectively; $p<0.001$) compared to the NO-CAD group. The two groups, instead, showed no significant differences in the presence of ST-segment and/or T-wave alterations on standard ECG on admission, as well as in peak of troponin T serum levels ($p=0.075$), and NT-pro-BNP levels ($p=0.43$) (Table I).

In patients with available data, the time intervals from the peak serum level of troponin T and a reduction of serum troponin T concentration >20% and >50%, compared to the peak level, were similar in the two groups (Figure 1).

In the CAD group, angiography showed one-vessel disease in 18 patients (34%), two-vessel disease in 17 (32%) and three-vessel disease in 18 (34%). In the NOCAD group, angiography showed normal coronary arteries in 41 patients (85.4%).

The diagnostic work-up during hospital staying in the latter group led to heterogeneous final diagnoses at discharge, which included myocarditis in 10 patients (20.1%), takotsubo disease in 9 (18.8%), chest pain related to paroxysmal tachyarrhythmias in 3 (6.3%), endocarditis in 1 (2.1%) and myocardial infarction with normal coronary arteries (MINOCA) in 25 patients (52.1%).

Table I. Main clinical characteristics of two groups of patients diagnosed with no-ST-segment elevation acute myocardial infarction on admission.

	CAD (No=53)	Group NOCAD (No=48)	Group *p*
Age (years)	67.8±11	58.3±15	0.001
Male sex	37 (69.8%)	23 (47.9%)	0.028
BMI (kg/m^2)	27.7±5.2	25.2±4.0	0.008
Cardiovascular risk factors			
Family hystory of CAD	14 (26.4%)	9 (18.8%)	0.48
Diabetes mellitus	13 (24.5%)	1 (2.1%)	0.001
Hypertension	41 (77.4%)	19 (39.6%)	0.000
Smoking	31 (58.5%)	27 (56.2%)	0.84
Hypercholesterolemia	25 (47.2%)	12 (25.0%)	0.024
Drug Therapy on admission			
Beta-blockers	13 (24.5%)	6 (12.5%)	0.14
Calcium-antagonists	11 (20.8%)	1 (2.1%)	0.004
ACEI/AT-II antagonists	21 (39.6%)	5 (10.4%)	0.001
Statins	13 (24.5%)	6 (12.5%)	0.14
Diuretics	4 (7.5%)	2 (4.2%)	0.680
Antidiabetics	13 (24.52%)	1 (2.1%)	0.001
Aspirin	9 (17.0%)	0 (0.0%)	0.003
Typical chest pain	35 (71.4%)	14 (28.6%)	<0.001
ST-segment depression	19 (35.8%)	11 (22.9%)	0.19
T wave alterations	9 (17.0%)	7 (14.6%)	1.00
Maximal troponin T (ng/ml)	13.45±21.42	7.11±12.34	0.075
NT-pro-BNP (pg/ml)*	783 (259-4171)	542 (123-3660)	0.43

ACEI=Angiotensin converting enzyme inhibitors; AT-II=angiotensin II; CAD=coronary artery disease. *Median and interquartile range.

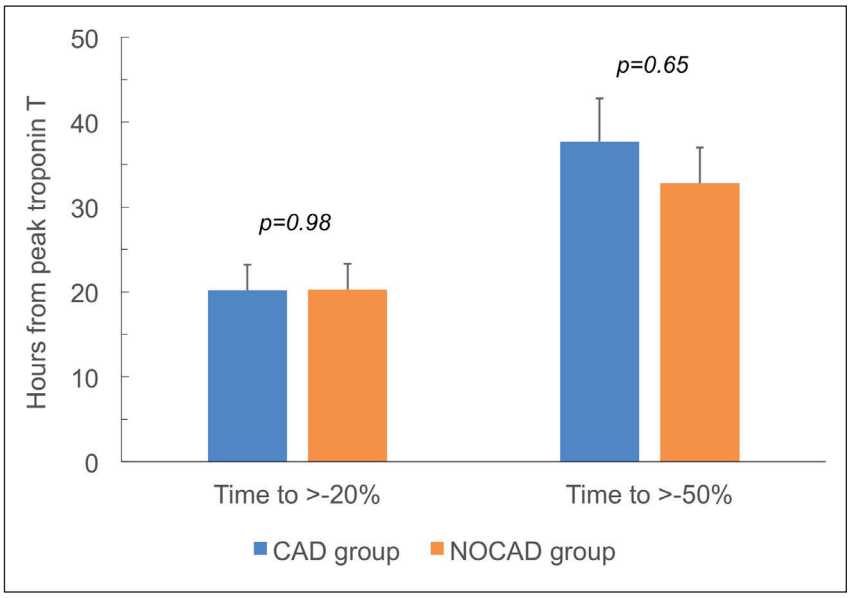

Figure 1. Time interval from peak troponin T concentration and detection of a decrease in troponin T levels >20% and >50% of the peak value in patients with CAD and NOCAD. Data refer to 33 and 34 patients of the two groups, respectively, for time interval to a decrease >20% and to 19 and 20 patients of the two groups, respectively, for time interval to a decrease >50%.

Echocardiographic Data

Divergences between the two echocardiographers about the presence of regional wall motion abnormalities occurred in 7 patients (6.9%), and controversies were solved by consensus. Overall, LVWMA of any kind were found in 28 patients (52.8%) in the CAD group and 21 patients (43.7%) in the NOCAD group (p=0.43). Specifically, one or more akinetic segments were detected in 14 (26.4%) and 13 (27.0%) patients, respectively, whereas one or more hypokinetic segments were detected in 14 (26.4%) and 8 (16.7%) patients, respectively. A detailed distribution of LVWMA (akinetic segments in the upper graph and hypokinetic segments in the bottom graph) in the two groups of patients is shown in Figure 2. No significant differences were found between the CAD and NOCAD groups in WMSI, both in the whole population (1.21±0.32 *vs.* 1.16±0.26, respectively; p=0.39) and in the subgroups of patients with LVWMA (1.41±0.40 *vs.* 1.38±0.27, respectively; p=0.74). No significant difference was found between the two groups in LVEF (54.7±9.8 *vs.* 56.4±6.8 %, respectively; p=0.30). The presence of LVWMA in the CAD group was independent of the severity of obstructive CAD at angiography (55.6%, 58.8% and 44.4% in patients with 1, 2 or 3-vessel CAD; p=0.65).

Multivariable Analysis

The results of multivariable logistic regression analysis for the presence of obstructive CAD are summarized in Table II. As shown, older age, male gender, typical angina, diabetes and hypertension, but not maximal TnT level were independent predictors of obstructive CAD in our patients.

Discussion

Our data show that performing an echocardiographic examination in patients with a suspect of first NSTEMI, based on the presence of chest pain and increased high-sensitivity troponin T serum levels, does not significantly help distinguish those with athero-thrombotic NSTEMI from those with NOCAD. Regional LVWMA were indeed found in 52.8% and 43.8% of patients with athero-thrombotic CAD and NOCAD, respectively, while both LVEF and WMSI were similar in the two groups. With the advent of the universal definition of acute myocardial infarction, the detection of increased levels of troponin in the serum has become central for the diagnosis, based on the hypothesis that troponin release, in the presence of symptoms and/or ischemic ECG changes, is specific of ischemic cardiomyocyte necrosis[1]. In recent years it has become clear that increased troponin levels are far from being an accurate marker of ischemic myocardial necrosis. Non-ischemic myocardial damage[5,11-13], but also transient myocardial ischemia without necrosis[14,15], might indeed result in troponin increase. Moreover, the accuracy of troponin increase for the diagnosis of acute myocardial infarction becomes progressively

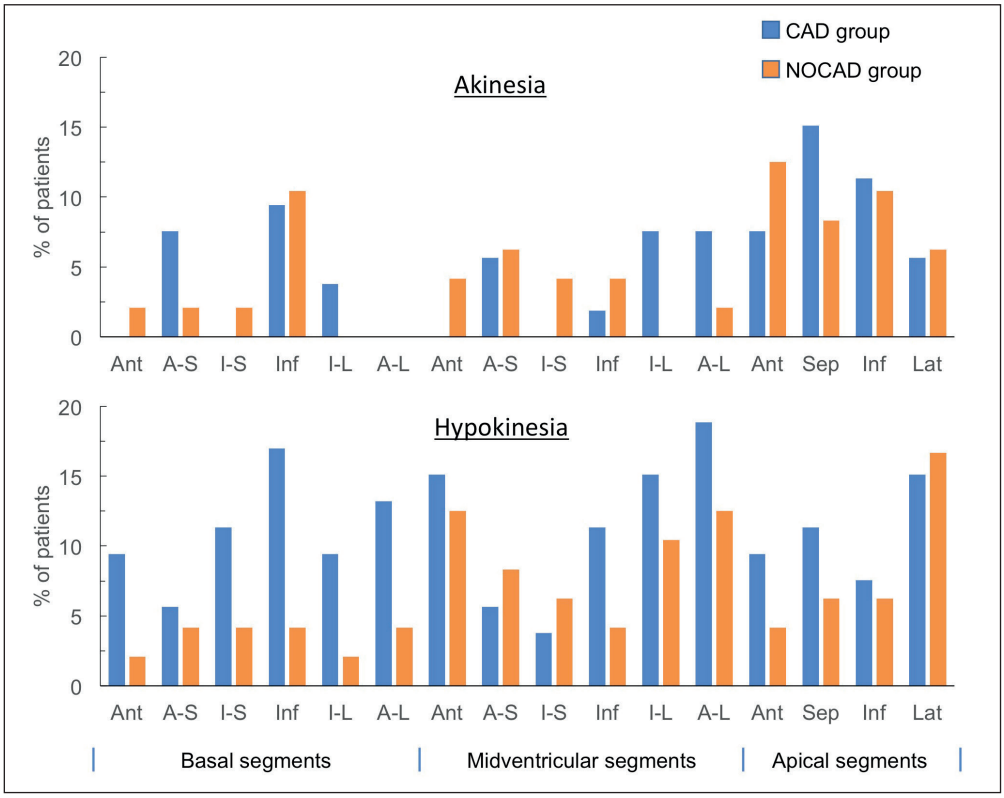

Figure 2. Distribution of akinetic segments *(upper graph)* and hypokinetic segments *(bottom graph)* of the left ventricle in the 2 groups of patients. Ant=anterior; A-L=antero-lateral; A-S=anteroseptal; Inf=inferior; I-L=infero-lateral; I-S=infero-septal; Lat=lateral; Sep=septal.

lower with increasing age and impairment of renal function[16]. Clinical guidelines recommend early coronary angiography and coronary revascularization in patients with a diagnosis of NSTEMI patients based on the detection of increased troponin levels[2-4]. Sizeable false positive diagnoses, however, may expose patients to the avoidable risk of invasive procedures, besides the unjustified increased costs related to inappropriate invasive management. Echocardiographic examination is increasingly required and performed in the emergency room to detect new wall motion abnormalities that, in patients with acute chest pain, might give support to the diagnosis of myocardial ischemic necrosis, in particular in doubtful cases as those of patients with only mild troponin increase. No study has consistently demonstrated the clinical utility of echocardiography in this clinical setting. Our data show that

Table II. Results of multivariate logistic regression analysis.

	Odds ratio	95% confidence interval	*p*
Typical angina	8.69	2.59-29.2	<0.001
Male gender	8.07	2.25-28.9	0.001
Hypertension	5.13	1.51-17.4	0.009
Age	1.06	1.01-1.11	0.023
Diabetes mellitus	16.4	1.24-217.0	0.034
Hypercholesterolemia	3.15	0.94-10.5	0.063
Maximal troponin T level	1.02	0.98-1.07	0.30
Body mass index	0.98	0.85-1.14	0.82

echocardiography seems, in fact, unable to give valuable support to the clinician in identifying, among patients with a suspect of first NSTEMI, those who have athero-thrombotic CAD at angiography. The reasons for the poor diagnostic yield of echocardiography are likely various. Regional LVWMA may occur in patients with cardiac diseases different from myocardial infarction caused by athero-thrombotic disease, including myocarditis, takotsubo disease, tachy-cardiomyopathy, or myocardial stunning or injury related to epicardial or microvascular coronary spasm. On the other side, the lack of any significant LVWMA at echocardiographic examination in about a half of patients with significant obstructive CAD might be explained with a limited sensitivity of the technique in patients with very small myocardial damage. Our data are at variance with those of a previous study[17] that showed an additional diagnostic value of echocardiography in patients admitted with a suspect of acute coronary syndrome. Differences in inclusion criteria and use of high-sensitive *vs*. standard assays for troponin measurements might, at least in part, account for the different results, in agreement with recent observations[18]. A relevant finding of our study is the high proportion, about a half of patients, that were found to have NOCAD in our population. This proportion is considerably higher than that reported in previous studies[6,7] and in a recent meta-analysis, that showed a prevalence of 6%. The reasons for this discrepancy might lie in the inclusion, in our work, of patients with the first episode of acute chest pain only, in the use of high-sensitive troponin T assay, and in the systematic invasive approach pursued in our hospital in patients with troponin increase, in agreement with international guideline recommendations[19]. Of note, looking at a typical rise and fall of serum troponin T levels did not seem helpful to distinguish between the two groups of patients, as a similar temporal decrease of troponin T concentrations was observed. From a clinical perspective, the high rate of NOCAD in our patients suggests that other variables should carefully be evaluated in patients presenting with acute chest pain and troponin increase to achieve a likely diagnosis of classical NSTEMI and trigger invasive assessment. In this regard, our data indicate, in agreement with previous reports[6-8,20], that careful assessment of symptoms, together with age, gender and cardiovascular risk factors, may give substantial help in guiding clinical management. Of note, specific final cardiac diagnoses other than NSTEMI were achieved during diagnostic work-up in about a half of NOCAD cases, whereas a diagnosis of myocardial infarction with NOCAD (MINOCA), related to epicardial and/or microvascular spasm, was the final diagnosis in the other half of patients, in agreement with previous studies[6-8,20]. Whether troponin increase actually reflects ischemic myocardial necrosis in the latter group of patients, remains to be determined[11-15,21].

Conclusions

We showed that performing the standard echocardiographic study in patients with a suspect of first NSTEMI is not helpful to identify those who are found to have significant atherothrombotic CAD at angiography.

Conflict of Interests

The authors declare that they have no conflict of interest.

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