Patients with Non-ST-Segment Elevation Myocardial Infarction Present with More Severe Systolic and Diastolic Dysfunction Than Patients with Unstable Angina

Nithima Chaowalit MD*, Ruedeekorn Auesethasak, MD*,
Yingsak Santanakorn MD*, Decho Jakrapanichakul MD*,
Maytinee Kittipovanonth MD*, Srisakul Chirakarnjanakorn MD*

** Division of Cardiology, Department of Medicine, Siriraj Hospital, Faculty of Medicine, Mahidol University, Bangkok, Thailand*

Background*: Patients with non ST-segment elevation acute coronary syndrome (NSTEACS) present with diverse clinical, electrocardiographic, cardiac biomarker, echocardiographic and angiographic characteristics. We sought to determine whether there was any difference in the indices of left ventricular systolic and diastolic function among subgroups of patients with NSTEACS.*

Material and Method: *We studied 121 consecutive patients (mean age 68.6 $\pm$ 11.3 years, 45% male) with NSTEACS who underwent comprehensive echocardiography within 48 hours of admission. Two-dimensional and Doppler echocardiography was performed for the evaluation of left ventricular systolic and diastolic function.*

Results: *Non ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA) were reported in 59% and 41% of patients, respectively. Clinical characteristics (such as age, gender, cardiovascular risk factors, prior myocardial infarction and revascularization, medication) were not significantly different between patients with NSTEMI and UA. Patients with NSTEMI were more likely to have wall motion abnormalities and lower left ventricular ejection fraction ($p < 0.05$) as compared to those with UA. Diastolic dysfunction was significantly more frequent and more severe in patients with NSTEMI than in those with UA.*

Conclusion: *Among patients with NSTEACS, left ventricular systolic and diastolic dysfunction was more frequent and more severe in patients with NSTEMI that in those with UA. These findings may be used to characterize the sicker group among patients with NSTEACS.*

Keywords*: Diastolic dysfunction, Echocardiography, Non ST-segment elevation myocardial infarction, Unstable angina*

J Med Assoc Thai 2011; 94 (Suppl. 1): S19-S24
Full text. e-Journal: *http://www.mat.or.th/journal*

Patients with non ST-segment elevation acute coronary syndrome (NSTEACS) present with diverse clinical, electrocardiographic (ECG), cardiac biomarker, echocardiographic and angiographic characteristics. Echocardiography has been used for diagnosis and risk assessment in patients presenting with symptoms suggestive of myocardial ischemia. Two-dimensional echocardiography provides the assessment of wall motion abnormalities and has been used for the detection of myocardial ischemia and infarction in patients with acute chest pain syndrome, regardless of the ECG findings on presentation. Tissue Doppler imaging (TDI), a recently developed echocardiographic modality, is useful for the evaluation of left ventricular (LV) systolic and diastolic function, regardless of loading conditions. It has several advantages over conventional echocardiography, including the better determination of myocardial velocities and a good correlation with invasive measures of ventricular systolic and diastolic function such as maximum or minimum dP/dt and time constant of LV relaxation. Therefore, the combination of information obtained by conventional echocardiography and TDI provides the

Correspondence to:
Chaowalit N, Division of Cardiology, Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
Phone: 0-2412-7000 ext. 6104, Fax: 0-2412-7412
E-mail: sincw@mahidol.ac.th

comprehensive evaluation of LV function. We sought to determine whether there was any difference in the indices of systolic and diastolic function among subgroups of patients with NSTEACS.

Material and Method

Study Population

Patients with the diagnosis of NSTEACS were consecutively enrolled into the study. The study was approved by the ethical committee of Siriraj Hospital. Patients had to be ≥ 18 years of age and had symptoms consistent with acute coronary syndrome accompanied by cardiac biochemical markers or ECG changes. Patients with Non-ST-segment Elevation Myocardial Infarction (NSTEMI) were defined as those with positive cardiac biochemical markers of necrosis accompanied by ST-segment changes, but without new ST-segment elevation on the index ECG. Patients with unstable angina (UA) were those who had ST-T wave changes on the index ECG, regardless of the presence of chest pain at the time of the ECG, with normal levels of cardiac biochemical markers of necrosis. Patients were excluded from the study if they had a ST-segment elevation myocardial infarction or new left bundle branch block, a permanent pacemaker, significant valvular heart disease, prosthetic valve replacement, underwent coronary revascularization within 48 hours of admission or if ECG showed right and left bundle branch block. Information about conventional coronary risk factors was obtained. Diabetes mellitus was defined according to the requirement for treatment with insulin or oral hypoglycemic agents, or a fasting plasma glucose ≥ 126 mg/dl on at least two occasions. Hypertension was defined from the history or an in-hospital systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mm Hg. Patients were considered to have dyslipidemia if they were receiving lipid-lowering agents or if their total cholesterol during hospitalization was ≥ 200 mg/dl, low-density lipoprotein cholesterol ≥ 130 mg/dl or high-density lipoprotein cholesterol < 40 mg/dl. Family history of premature coronary artery disease was defined as the presence of coronary artery disease in a first-degree relative for male age < 55 years or female < 65 years.

Echocardiography

All patients with NSTEACS underwent comprehensive echocardiography within 48 hours of admission. Echocardiographic examination consisted of two-dimensional, M-mode, conventional Doppler, and TDI measurements. All echocardiographic parameters were reported as the average of the values of at least 3 consecutive beats. The echocardiographers (NC, RA and YS) were blinded to the final diagnosis. LV ejection fraction was determined using the Modified Simpson's rule (biplane). LV systolic dysfunction was defined as the LV ejection fraction < 40%. LV diastolic function was evaluated by Doppler echocardiography of transmitral flow velocities and TDI of medial mitral annulus. Pulse-wave Doppler study of mitral valve inflow was determined by placing sample volume at the tip of mitral leaflets in the apical 4-chamber view. Peak early (E) and late diastolic velocities of mitral inflow and deceleration time of E were then measured. The TDI determination of diastolic function was performed in apical 4-chamber view with the sample volume at the septal aspect of mitral annulus. Longitudinal early (E') and late diastolic myocardial velocities were measured. E/E' ratio was defined as high if E/E' ratio was > 15, indicating the elevation of LV end-diastolic pressure. Left atrial volume (LAV), indicating the chronicity of diastolic dysfunction, was measured using the area-length biplane method. LA enlargement was defined as LAV index ≥ 32 ml/M^2.

Statistical Analysis

Categorical variables were summarized as percent (%) of patients, and continuous variables as mean ± standard deviation. Comparison between groups was based on the independent sample t-test and the Mann-Whitney U test for continuous variables and Pearson's Chi-square test for categorical variables. Data were analyzed using SPSS for Windows (Version 11.5, SPSS Inc., Chicago, Illinois, USA). A p-value < 0.05 was considered statistically significant.

Results

There were 121 patients with NSTEACS enrolled in the study. NSTEMI and UA were diagnosed in 71 (59%) and 50 (41%) patients, respectively. The mean age was 68.6 ± 11.3 years and 45% were male gender. Cardiovascular risk factors were described as hypertension in 85%, dyslipidemia in 67%, diabetes mellitus in 64%, smoking in 11% and family history of premature coronary artery disease in 2% of patients. Prior myocardial infarction and coronary revascularization were reported in 21% and 25% of patients, respectively. Dyspnea at presentation and/or clinical heart failure (Killip class > 1) was presented in 61% of patients. Clinical characteristics (such as age, gender, cardiovascular risk factors, prior myocardial infarction and revascularization, medication) were not

significantly different between patients with NSTEMI and UA (Table 1).

Echocardiographic Findings

The mean LV ejection fraction was 55.2 ± 14.6%. LV systolic dysfunction and regional wall motion abnormalities were present in 17% and 62% of patients, respectively. LV systolic dysfunction was more prevalent in patients with NSTEMI than in those with UA (22.5% and 8.0% of patients, respectively, p = 0.03). Patients with NSTEMI had lower LV ejection fraction than those with UA (51.8 ± 14.9% vs. 60.2 ± 12.9%, p = 0.002). Diastolic function was categorized as normal, grade 1 = abnormal relaxation, grade 2 = pseudonormalization pattern and grade 3 = restrictive filling pattern in 5%, 67%, 22% and 6% of patients, respectively. High E/E' ratio, indicating the elevation of LV end-diastolic pressure, was found in 66% of patients. The mean LAV and LAV index were 64.4 ± 20.8 ml and 39.8 ± 13.0 ml/M^2, respectively. LA enlargement was detected in 71% of patients. Diastolic dysfunction was more frequent and more severe in patients with NSTEMI than in those with UA as shown in Table 2. Furthermore, most of parameters showing diastolic dysfunction (E', E/E' and deceleration time) remained more severe in patients with NSTEMI after adjusted for LV ejection fraction ($p < 0.001$).

Discussion

The present study shows the differences in the echocardiographic findings among the subgroups of patients with NSTEACS. The echocardiographic characteristics in patients with NSTEMI and UA were significantly different both in term of frequency and severity of LV systolic and diastolic dysfunction.

Among the subgroups of patients with NSTEACS, patients with NSTEMI represent the more severe form of the underlying coronary artery occlusion and myocardial injury than those with UA. This may lead to a variety of clinical and laboratory findings. Previous studies have shown several parameters used to risk stratify patients with NSTEACS, such as clinical, ECG, cardiac biomarkers, echocardiographic and angiographic characteristics.

Table 1. Baseline characteristics of patients with NSTEMI and UA

	NSTEMI	UA	p-value
Age (year)	69.1 ± 10.6	67.8 ± 12.4	0.87
Male gender	34 (47.9%)	21 (42.0%)	0.52
Diabetes mellitus	48 (67.6%)	29 (58.0%)	0.28
Hypertension	61 (85.9%)	42 (84.0%)	0.77
Dyslipidemia	47 (66.2%)	34 (68.0%)	0.84
Smoking	10 (14.1%)	3 (6.0%)	0.16
Prior myocardial infarction	17 (23.9%)	8 (16.0%)	0.29
Prior revascularization	16 (22.5%)	14 (28.0%)	0.49

Data are expressed as mean ± standard deviation and the number (%) of patients

Table 2. Indices of diastolic function in patients with NSTEMI and UA

	NSTEMI	UA	p-value
E (cm/s)	100.3 ± 11.8	74.6 ± 14.3	0.03
E' (cm/s)*	3.0 (1.0, 15.0)	4.5 (1.0, 18.0)	< 0.001
E/E' ratio*	22.6 (5.7, 68.7)	15.0 (3.1, 49.0)	< 0.001
E/E' ratio > 15	56 (80)	25 (52)	0.001
DT (ms)	201.2 ± 90.8	245.2 ± 87.0	0.006
LAV (ml)	67.3 ± 20.4	60.2 ± 20.8	0.05

Data are expressed as mean ± standard deviation, median (min, max) and the number (%) of patients. * Compare median using the Mann-Whitney U test. DT = deceleration time, E = early transmitral flow velocity, E' = early diastolic septal mitral annulus velocity, LAV = left atrial volume

TIMI risk score is one of the examples for risk stratification among patients with NSTEACS, using the combination of various parameters, such as clinical setting, ST-segment deviation and cardiac marker, to categorize the risk of death and ischemic events[1].

In the setting of acute coronary syndrome, echocardiography is of paramount importance in the diagnosis and prognostication. Losses of myocardial contractile function/tissue and changes in ventricular geometry have been described in the setting of acute coronary syndrome. These abnormalities can modify LV systolic and diastolic function and furthermore, affect the clinical course. LV systolic dysfunction contributes to impaired LV pump function and leads to mortality and morbidity after acute myocardial infarction (AMI). Furthermore, LV diastolic dysfunction after AMI contributes to symptoms and disability associated with heart failure and even death. LV systolic function has long been a classic echocardiographic characteristic in determining the prognosis after AMI. Several previous studies showed that LV systolic dysfunction strongly predicted adverse clinical outcomes, such as mortality and heart failure, after AMI[2-6]. Most of such studies were conducted in patients with AMI and the majority was from patients with ST-segment elevation myocardial infarction. Information from the present study is unique in that it was obtained specifically from patients with NSTEACS, which includes both underlying pathology of myocardial infarction (represented by patients with NSTEMI) and myocardial ischemia (represented by patients with UA). The results showed that LV systolic dysfunction and the more advanced LV diastolic dysfunction were more prevalent in patients with NSTEMI than in those with UA, which may reflect the severity of underlying acute coronary pathology and extent of myocardial injury.

Diastolic dysfunction occurs early after acute coronary artery occlusion with or without LV systolic dysfunction. Several diastolic parameters assessed by transthoracic echocardiography have also been shown to be strong prognostic indicators after AMI[7-12]. LV diastolic dysfunction contributes to signs and symptoms of heart failure and mortality after AMI, regardless of LV systolic function. Data from previous studies showed that the more severe the diastolic dysfunction the worse the prognosis after AMI[7,8,12-14]. Therefore, an appropriate treatment to lessen the severity of diastolic dysfunction should improve the clinical outcomes after AMI. E/E' ratio, Doppler-derived deceleration time and LAV have reflected the severity of diastolic function. E/E' has been shown to be the most accurate non-invasive predictor of elevated LV filling pressure and pulmonary capillary wedge pressure[15] and high E/E' was associated with adverse outcomes and worse survival after AMI[7-9]. Short deceleration time has also been reported to be an important prognostic value after AMI and correlated with the well-documented prognostic value of clinical indicators of LV filling pressures, such as Killip class[9,12,16,17]. Previous study has found that myocardial ischemia resulted in significant LA dilation, depressed LA systolic function, and altered LA diastolic stiffness[18]. LAV has been described as an important predictor of survival after acute AMI[11,19]. The present study showed that among patients with NSTEACS, the more severe-group, patients with NSTEMI, presented more frequently with the more advanced LV diastolic dysfunction as described by shorter deceleration time, higher E/E' ratio and larger LAV. The study was exclusively conducted in patients with NSTEACS to echocardiographically differentiate those with NSTEMI and UA. These findings may have prognostic and therapeutic implications among the subgroup of patients with NSTEACS.

Study Limitations

The echocardiography was performed mostly in the intensive care unit and the in-patient medicine wards, not in the standard echocardiography laboratory and some of them were performed during out-of-office hours. Therefore, data regarding the inter-observer variability were not available.

Conclusion

Data from the present study demonstrate that, among patients with NSTEACS, LV systolic and diastolic dysfunction was more frequent and more severe in patients with NSTEMI that in those with UA. This may therefore assist in the risk stratification and clinical decision-making of patients with NSTEACS.

Potential conflicts of interest

None.

References

1. Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. JAMA 2000; 284: 835-42.
2. Hellermann JP, Jacobsen SJ, Redfield MM, Reeder

GS, Weston SA, Roger VL. Heart failure after myocardial infarction: clinical presentation and survival. Eur J Heart Fail 2005; 7: 119-25.
3. Velazquez EJ, Francis GS, Armstrong PW, Aylward PE, Diaz R, O'Connor CM, et al. An international perspective on heart failure and left ventricular systolic dysfunction complicating myocardial infarction: the VALIANT registry. Eur Heart J 2004; 25: 1911-9.
4. Nicod P, Gilpin E, Dittrich H, Chappuis F, Ahnve S, Engler R, et al. Influence on prognosis and morbidity of left ventricular ejection fraction with and without signs of left ventricular failure after acute myocardial infarction. Am J Cardiol 1988; 61: 1165-71.
5. White HD, Norris RM, Brown MA, Brandt PW, Whitlock RM, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. Circulation 1987; 76: 44-51.
6. Weir RA, McMurray JJ, Velazquez EJ. Epidemiology of heart failure and left ventricular systolic dysfunction after acute myocardial infarction: prevalence, clinical characteristics, and prognostic importance. Am J Cardiol 2006; 97: 13F-25F.
7. Moller JE, Sondergaard E, Poulsen SH, Egstrup K. Pseudonormal and restrictive filling patterns predict left ventricular dilation and cardiac death after a first myocardial infarction: a serial color M-mode Doppler echocardiographic study. J Am Coll Cardiol 2000; 36: 1841-6.
8. Nijland F, Kamp O, Karreman AJ, van Eenige MJ, Visser CA. Prognostic implications of restrictive left ventricular filling in acute myocardial infarction: a serial Doppler echocardiographic study. J Am Coll Cardiol 1997; 30: 1618-24.
9. Hillis GS, Moller JE, Pellikka PA, Gersh BJ, Wright RS, Ommen SR, 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: 360-7.
10. Sakata K, Kashiro S, Hirata S, Yanagisawa A, Ishikawa K. Prognostic value of Doppler transmitral flow velocity patterns in acute myocardial infarction. Am J Cardiol 1997; 79: 1165-9.
11. Moller JE, Hillis GS, Oh JK, Seward JB, Reeder GS, Wright RS, et al. Left atrial volume: a powerful predictor of survival after acute myocardial infarction. Circulation 2003; 107: 2207-12.
12. Moller JE, Egstrup K, Kober L, Poulsen SH, Nyvad O, Torp-Pedersen C. Prognostic importance of systolic and diastolic function after acute myocardial infarction. Am Heart J 2003; 145: 147-53.
13. Whalley GA, Gamble GD, Doughty RN. Restrictive diastolic filling predicts death after acute myocardial infarction: systematic review and meta-analysis of prospective studies. Heart 2006; 92: 1588-94.
14. Poulsen SH, Moller JE, Norager B, Egstrup K. Prognostic implications of left ventricular diastolic dysfunction with preserved systolic function following acute myocardial infarction. Cardiology 2001; 95: 190-7.
15. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. Circulation 2000; 102: 1788-94.
16. Risk stratification and survival after myocardial infarction. N Engl J Med 1983; 309: 331-6.
17. Temporelli PL, Giannuzzi P, Nicolosi GL, Latini R, Franzosi MG, Gentile F, et al. Doppler-derived mitral deceleration time as a strong prognostic marker of left ventricular remodeling and survival after acute myocardial infarction: results of the GISSI-3 echo substudy. J Am Coll Cardiol 2004; 43: 1646-53.
18. Stefanadis C, Dernellis J, Tsiamis E, Toutouzas P. Effects of pacing-induced and balloon coronary occlusion ischemia on left atrial function in patients with coronary artery disease. J Am Coll Cardiol 1999; 33: 687-96.
19. Beinart R, Boyko V, Schwammenthal E, Kuperstein R, Sagie A, Hod H, et al. Long-term prognostic significance of left atrial volume in acute myocardial infarction. J Am Coll Cardiol 2004; 44: 327-34.

ผู้ป่วยกล้ามเนื้อหัวใจตายเฉียบพลันชนิด ST ไม่ยก มีความผิดปกติในการบีบตัวและคลายตัวของกล้ามเนื้อหัวใจแบบรุนแรงกว่าผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดแบบ unstable angina

นิธิมา เชาวลิต, ฤดีกร เอื้อเศรษฐศักดิ์, ยิ่งศักดิ์ สันธนาฑร, เดโช จักราพานิชกุล, เมทินี กิตติโพวานนท์, ศรีสกุล จิรกาญจนากร

ภูมิหลัง: *ผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันชนิด ST ไม่ยก (NSTEACS) มีความหลากหลายในหลายด้านได้แก่ อาการทางคลินิก คลื่นไฟฟ้าหัวใจ ค่าเอนไซม์กล้ามเนื้อหัวใจ ผลการตรวจคลื่นเสียงสะท้อน หัวใจและการฉีดสีหลอดเลือดหัวใจ จุดประสงค์ของการศึกษานี้เพื่อหาความแตกต่างของตัวแปรที่บ่งชี้การ บีบตัวและคลายตัวของกล้ามเนื้อหัวใจในผู้ป่วยกลุ่มย่อยของผู้ป่วย NSTEACS*

วัสดุและวิธีการ: *ผู้ป่วย NSTEACS จำนวน 121 คน (อายุเฉลี่ย 68.6 ปี เพศชายร้อยละ 45) ได้รับการตรวจคลื่นเสียงสะท้อนหัวใจภายใน 48 ชั่วโมง ที่รับเข้านอนในโรงพยาบาลศิริราช*

ผลการศึกษา: *มีผู้ป่วยโรคกล้ามเนื้อหัวใจตายเฉียบพลันชนิด ST ไม่ยก (NSTEMI) ร้อยละ 59 และผู้ป่วยโรคกล้ามเนื้อหัวใจขาดเลือดแบบ unstable angina (UA) ร้อยละ 41 และไม่พบความ แตกต่างของข้อมูลพื้นฐานทางคลินิกระหว่าง 2 กลุ่ม ผู้ป่วยกลุ่ม NSTEMI มีความผิดปกติของ กล้ามเนื้อหัวใจบางตำแหน่ง และการบีบตัวของหัวใจลดลงกว่าปกติมากกว่าในผู้ป่วยกลุ่ม UA ผู้ป่วยกลุ่ม NSTEMI พบความผิดปกติในการคลายตัวของหัวใจได้บ่อย และรุนแรงกว่าผู้ป่วยกลุ่ม UA*

สรุป: *ผู้ป่วยกลุ่ม NSTEMI พบความผิดปกติในการบีบตัวและคลายตัวของหัวใจได้บ่อย และรุนแรงกว่าในผู้ป่วยกลุ่ม UA ข้อมูลนี้อาจเป็นประโยชน์ในการประเมินความเสี่ยงและการพยากรณ์โรคในผู้ป่วยกลุ่ม NSTEACS ได้*