One-Year Clinical Outcomes among Patients with Metabolic Syndrome and Acute Myocardial Infarction

Mi Seon Ji, MD¹, Myung Ho Jeong, MD¹,¹³, Youngkeun Ahn, MD¹,¹³, Young Jo Kim, MD², Shung Chull Chae, MD³, Taek Jong Hong, MD³, In Whan Seong, MD³, Jei Keon Chae, MD⁶, Chong Jin Kim, MD⁴, Myeong Chan Cho, MD⁸, Seung-Woon Rha, MD³, Jang Ho Bae, MD¹⁰, Ki Bae Seung, MD¹¹, Seung Jung Park, MD¹², and Other Korea Acute Myocardial Infarction Registry Investigators

¹Chonnam National University Hospital, Gwangju, ²Yeungnam University Hospital, Daegu, ³Kyungpook National University Hospital, Daegu, ⁴Pusan National University Hospital, Busan, ⁵Chungnam National University Hospital, Daejeon, ⁶Chonbuk National University Hospital, Jeonju, ⁷Kyung Hee University Hospital, Seoul, ⁸Chongbuk National University Hospital, Cheongju, ⁹Korea University Guro Hospital, Seoul, ¹⁰Konyang University, Daejeon, ¹¹The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, ¹²Asan Medical Center, Seoul, ¹³Korea Cardiovascular Stent Research Institute of Chonnam National University, Gwangju, Korea

Background and Objectives: Metabolic syndrome (MetS) is an important risk factor for cardiovascular disease. However, the clinical outcome of acute myocardial infarction (AMI) with MetS has not been well examined. The purpose of this study was to evaluate the clinical outcomes of AMI patients with MetS.

Subjects and Methods: We evaluated a total of 6352 AMI patients who had successful percutaneous coronary interventions and could be identified for MetS between 2005 and 2008 at 51 hospitals participating in the Korea Acute Myocardial Infarction Registry. They were divided into 2 groups according to the presence of MetS: the MetS group (n=2493, 39.2%) versus the Non-MetS group (n=3859, 60.8%). In addition, 4049 AMI patients with high levels of low density lipoprotein-cholesterol (LDL-C) (≥100 mg/dL) among them, were divided into the MetS group (n=1561, 38.6%) versus the Non-MetS group (n=2488, 61.4%).

Results: In the overall population, there was no significant difference in 12-month the major adverse cardiac events (MACE) rate between the 2 groups. However, the MetS group showed a significantly higher 12-month MACE rate in the high LDL-C population. Multivariate analysis showed that MetS was an independent prognostic factor for 12-month MACE (hazard ratio (HR) 1.607, 95% confidence interval (CI) 1.027 to 2.513, adjusted p=0.038) and for 12-month target vessel revascularization (HR 1.564, 95% CI 1.092 to 2.240, adjusted p=0.015) in the high LDL-C population.

Conclusion: MetS patients with AMI in the overall population showed no significant difference in 12-month clinical outcomes. However, in patients with higher LDL-C ≥100 mg/dL, they showed significantly worse clinical outcome than Non-MetS patients. Therefore, it is important to ascertain the presence of MetS in AMI patients, and more aggressive therapy should be strongly considered for AMI patient with MetS. (Korean Circ J 2013;43:519-526)

KEY WORDS: Metabolic syndrome; Myocardial infarction; Low density lipoprotein-cholesterol.
Metabolic syndrome (MetS) is a major cause of AMI, with a rapidly increasing tendency in prevalence. It has multiple cardiovascular risk factors consisting of abdominal obesity, high blood pressure, impaired blood glucose, high triglyceride, and a low level of high density lipoprotein-cholesterol (HDL-C). There have been many studies of the relationship between MetS and cardiovascular disease. However, there remains controversy over the impact of MetS on prognosis after AMI. Furthermore, there have been relatively few studies of the impact of MetS on patients with a high level of low density lipoprotein-cholesterol (LDL-C) (more than 100 mg/dL), who have been known to be associated with an increased risk of AMI among Asian populations.

Therefore, our study investigated the impact of MetS on the long-term prognosis among AMI patients who underwent successful percutaneous coronary intervention (PCI), especially in patients with high levels of LDL-C (more than 100 mg/dL), using the database of the Korea Acute Myocardial Infarction Registry (KAMIR).

Subjects and Methods

Patient population
We evaluated a total of 6352 AMI patients who had successful PCI and could be identified for the presence of MetS between November 2005 and January 2008 at 51 hospitals participating in the KAMIR. They were divided into 2 groups according to the presence of MetS: the MetS group (n=2493, 39.2%) versus the Non-MetS group (n=3859, 60.8%). Among them, 4049 AMI patients who had high levels of LDL-C (more over 100 mg/dL) were selected and divided into the MetS group (n=1561, 38.6%) versus the Non-MetS group (n=2488, 61.4%). The patient flow chart is shown in Fig. 1.

The KAMIR is the largest multicenter data collection registry in Korea, designed to evaluate the outcomes of AMI patients. The KAMIR included 51 community and teaching hospitals and contained data for AMI patients from November 2005 to January 2008.

The diagnosis of AMI was based on a clinical symptom consistent with AMI and at least one of the following: specific changes on the electrocardiography, serial increases of serum cardiac markers of myocardial necrosis, and/or an angiographic finding of coronary artery disease (CAD). For the diagnosis of MetS, we used modified National Cholesterol Education Program-Adult Treatment Panel III criteria. The diagnostic criteria for MetS were elevated blood pressure (systolic ≥130 mm Hg, or diastolic ≥85 mm Hg) or drug treatment for hypertension; impaired blood glucose or drug treatment for elevated glucose or a history of diabetes; reduced HDL-C (<40 mg/dL in men, <50 mg/dL in women) or drug treatment for dyslipidemia; elevated triglyceride (≥150 mg/dL) or drug treatment for dyslipidemia; and abdominal obesity (waist circumference >90 cm in men and >80 cm in women). Our study included a history of drug treatment for hypertension instead of blood pressure and a history of drug treatment for diabetes instead of blood glucose for the diagnosis of MetS. Coronary artery angiography and stent insertion were performed using standard methods. The decision for detailed treatment was left up to the physician’s discretion. A clinical follow-up was performed during a period of 12 months after enrollment.

Fig. 1. Patient flow chart. A total of 6352 AMI patients who had successful PCI and could be identified for MetS between November 2005 and January 2008 at 51 hospitals participating in the Korea Acute Myocardial Infarction Registry were divided into 2 groups according to the presence of MetS: the MetS group versus the Non-MetS group. Among them, 4049 AMI patients who had high LDL-C levels (more than 100 mg/dL) were divided into the MetS group versus the Non-MetS group. AMI: acute myocardial infarction, PCI: percutaneous coronary intervention, MetS: metabolic syndrome, LDL-C: low density lipoprotein-cholesterol.

The primary end points were cardiac death and a composite of major adverse clinical events (MACE) during the 12-month follow-up period. MACE included cardiac death, myocardial infarction, and target vessel revascularization (TVR). Cardiac death was defined as death from pump failure, arrhythmia, ventricular septal rupture, or free wall rupture.

Statistical analysis
The Statistical Package for the Social Sciences (SPSS) for Windows version 18.0 (SPSS Inc., Chicago, IL, USA) was used for all analyses. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), and compared with an independent t-test or Mann-Whitney U test. Categorical variables were expressed as percentage and compared with a chi-square test. Missing values were coded as “missing” in SPSS. Cox regression analysis was performed to analyze the independent impact of MetS on 12-month clinical outcomes in AMI patients who had undergone successful PCI. All variables with p<0.2 in univariate analysis were entered into a multivariate analysis. The results are presented as adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) and p. Co-variables, which were used to adjust for the difference in baseline characteristics in 12-month MACE, were age, gender, atypical symptoms, chest pain, low blood pressure, heart rate, cerebro-

http://dx.doi.org/10.4070/kcj.2013.43.8.519 www.e-kcj.org
vascular disease, smoking, multi-vessel disease, drug eluting stent (DES), left ventricular ejection fraction, creatinine clearance rate (CrCl), N-terminal pro-B type natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hsCRP), troponin T, heparin, glycoprotein IIb/IIIa (GP2b3a) inhibitors, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, beta blockers, calcium channel blockers (CCBs), and statin.

All variables were considered to be statistically significant when the p was less than 0.05.

**Ethics statement**

Our study was conducted according to the Declaration of Helsinki. The study protocol was approved by the institutional review board of all centers, and the approval number was 05-49 of Chonnam Na-

**Table 1. Baseline clinical characteristics**

| Variables               | MetS (n=2493)          | No–MetS (n=3859)         | p     |
|-------------------------|------------------------|--------------------------|-------|
| Age (years)*            | 65.2 (55.6, 72.6)      | 62.8 (52.5, 71.6)        | <0.001|
| Men                     | 1412 (56.6)            | 3010 (78.1)              | <0.001|
| Diabetes                | 1454 (58.5)            | 607 (15.7)               | <0.001|
| Hypertension            | 2001 (80.4)            | 1544 (40.0)              | <0.001|
| Dyslipidemia            | 294 (13.9)             | 305 (9.0)                | <0.001|
| Previous CAD            | 203 (8.1)              | 189 (4.9)                | <0.001|
| Smoker                  | 1237 (49.8)            | 2517 (65.5)              | <0.001|
| Family history          | 174 (7.8)              | 271 (7.7)                | 0.900 |
| Chest pain              | 2108 (86.1)            | 3312 (86.7)              | 0.538 |
| Atypical symptoms       | 333 (13.4)             | 428 (11.1)               | 0.007 |
| Symptom to door time    | 278 (130,895)          | 257 (120,782)            | 0.013 |
| Door to balloon time    | 609 (94,367)           | 282 (85,2763)            | <0.001|
| SBP (mm Hg)             | 130.7±29.81            | 128.4±30.92              | 0.003 |
| Waist circumference (cm)| 94.9±57.3              | 91.0±65.7                | 0.016 |
| LVEF (%)                | 52.0±12.14             | 52.1±13.31               | 0.864 |
| Killip class >II        | 297 (12.2)             | 370 (9.7)                | 0.002 |
| STEMI                   | 1498 (60.1)            | 2624 (68.0)              | <0.001|
| Total cholesterol (mg/dL)| 187.1±49.97           | 183.7±43.92              | 0.006 |
| LDL-C (mg/dL)           | 118.9±46.02            | 119.2±41.50              | 0.791 |
| HDL-C (mg/dL)           | 40.6±26.94             | 46.6±24.93               | <0.001|
| Triglycerides (mg/dL)   | 172.9±130.60           | 113.4±90.96              | <0.001|
| Glucose (mg/dL)         | 197.1±94.14            | 158.0±67.67              | <0.001|
| CrCl (mL/min)*          | 65.6 (46.0, 87.4)      | 70.9 (54.0, 89.7)        | <0.001|
| CK-MB* (ng/mL)          | 69.4 (18.0, 187.4)     | 101.4 (28.0, 232.2)      | <0.001|
| Troponin I (ng/mL)*     | 19.4 (3.9, 50.0)       | 22.8 (4.2, 53.1)         | 0.015 |
| hsCRP (mg/L)*           | 5.5 (1.8, 23.7)        | 4.6 (1.4, 18.8)          | <0.001|
| NT-proBNP (pg/mL)*      | 599.0 (144.0, 2224.5)  | 425 (102.0, 1493.8)      | <0.001|
| GP2b3aI                 | 287 (11.5)             | 510 (13.3)               | 0.046 |
| ACEI/ARB                | 2063 (83.1)            | 3134 (81.4)              | 0.104 |
| Beta-blockers           | 1920 (77.3)            | 2902 (75.4)              | 0.087 |
| CCB                     | 355 (14.3)             | 387 (10.1)               | <0.001|
| Statin                  | 1985 (79.9)            | 3074 (79.9)              | 0.980 |
| Complications           | 330 (13.3)             | 452 (11.8)               | 0.074 |

Data are presented as the n (%) of patients or mean±SD. *Values are expressed as the median (interquartile range). MetS: metabolic syndrome, CAD: coronary artery disease, SBP: systolic blood pressure, LVEF: left ventricular ejection fraction, STEMI: ST elevation myocardial infarction, LDL-C: low density lipoprotein-cholesterol, HDL-C: high density lipoprotein-cholesterol, CrCl: creatinine clearance, CK-MB: creatine kinase-MB, hsCRP: high-sensitivity C-reactive protein, NT-proBNP: N-terminal pro-B type natriuretic peptide, GP2b3a: glycoprotein IIb/IIIa inhibitor, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium channel blocker.
Results

Baseline characteristics

A total of 6352 patients were included in the overall population; 2493 (39.2%) patients with MetS and 3859 (60.8%) patients without MetS. Among them, a total of 4049 patients were included in the high LDL-C population (≥100 mg/dL); 1561 (38.6%) patients with MetS and 2488 (61.4%) patients without MetS.

The baseline characteristics are summarized in Table 1. In the overall population, compared to the Non-MetS group, the MetS group was older, more likely to be female, and had more atypical symptoms, a higher Killip class (class>II) and a higher tendency of non-ST-elevation myocardial infarction (NSTEMI). Both symptom to door time and door to balloon time were longer in the MetS group. The MetS group had more comorbidity factors, such as diabetes, hypertension, dyslipidemia, and a past history of CAD. In addition, hs-CRP and NT-proBNP were higher, but creatine kinase-MB and troponin I, and CrCl were lower in the MetS group. Triglyceride and blood sugar were higher and HDL-C was lower in the MetS group. There were no significant differences in the level of LDL-C between the 2 groups. Statin was similarly prescribed in both groups, but less GP2b3A inhibitor and more CCBs were prescribed in the MetS group.

Table 2. Coronary angiographic findings

| Variables                      | MetS (n=2493) | No-MetS (n=3859) | p   |
|--------------------------------|--------------|-----------------|-----|
| Culprit coronary artery        |              |                 |     |
| LAD                            | 1089 (43.7)  | 1835 (47.6)     | 0.003|
| LCX                            | 433 (17.4)   | 612 (15.9)      | 0.113|
| RCA                            | 928 (37.2)   | 1341 (34.7)     | 0.044|
| Left main                      | 37 (1.5)     | 66 (1.7)        | 0.489|
| Vessel number                  |              |                 |     |
| One vessel                     | 856 (34.5)   | 1766 (45.9)     | <0.001|
| Two vessel                     | 872 (35.1)   | 1191 (30.9)     | <0.001|
| Three vessel                   | 686 (27.6)   | 796 (20.7)      | <0.001|
| Left main                      | 69 (2.8)     | 96 (2.5)        | 0.491|
| ACC/AHA type                   |              |                 |     |
| Type A                         | 83 (3.6)     | 125 (3.4)       | 0.758|
| Type B1                        | 479 (20.5)   | 668 (18.2)      | 0.026|
| Type B2                        | 612 (26.3)   | 1020 (27.8)     | 0.179|
| Type C                         | 1157 (49.6)  | 1851 (50.5)     | 0.505|
| Pre-PCI TIMI                   |              |                 |     |
| TIMI 0                         | 999 (41.6)   | 1709 (45.4)     | 0.004|
| TIMI I                         | 277 (11.5)   | 395 (10.5)      | 0.196|
| TIMI II                        | 426 (17.8)   | 612 (16.3)      | 0.125|
| TIMI III                       | 696 (29.1)   | 1050 (27.9)     | 0.307|
| Lesion type B2/C               | 1769 (75.9)  | 2871 (78.4)     | 0.026|
| Pre-PCI TIMI 0/I               | 1276 (53.2)  | 2104 (55.9)     | 0.038|
| Post-PCI TIMI 0/I              | 27 (1.1)     | 28 (0.7)        | 0.123|
| Stent length                   | 25.4±6.34    | 25.2±6.32       | 0.222|
| Stent diameter                 | 3.14±0.43    | 3.17±0.44       | 0.004|
| Stent number                   | 1.6±0.91     | 1.5±0.85        | 0.001|

Data are presented as the n (%) of patients or mean±SD. MetS: metabolic syndrome, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery, ACC/AHA: American College of Cardiology/American Heart Association, PCI: percutaneous coronary intervention, TIMI: Thrombolysis in Myocardial Infarction.
American Heart Association lesion type, post-PCI TIMI flow grade, and stent sizes between the MetS and Non-MetS groups. The stent number was higher, and stent diameter was smaller in the MetS group.

Clinical outcomes at 12 months in patients with AMI

A total of 6352 patients were included in the overall population, and a total of 4049 patients among them were included in the high LDL-C population.

Clinical outcomes in the overall population and in the high LDL-C population are listed in Table 3 and 4. In the overall population, the in-hospital mortality rate was higher in the MetS group, but there was no significant difference. In addition, the 12-month MACE rates in the MetS group versus the Non-MetS groups of the overall population were 8.8% vs. 6.2%, respectively. The numbers of patients included in the final Cox regression analysis for the 12-month MACE rates were 1666 in the overall population, and there was no significant difference in the 12-month MACE rates (adjusted p=0.176) between the MetS group and Non-MetS groups (Table 3, Fig. 2). However, in the high LDL-C population, the 12-month MACE rates of the MetS group versus the Non-MetS group were 8.2% vs. 5.5%, and the 12-month TVR rates were 3.9% vs. 2.9%, respectively. The numbers of patients included in the final Cox regression analysis for the 12-month MACE rates in the high LDL-C population, and there was a significant difference in 12-month MACE rates (adjusted p=0.038) as well as 12-month TVR rates (adjusted p=0.015) (Table 4, Fig. 3).

Predictors of major adverse cardiovascular events

Multivariate analysis using the Cox proportional hazard model in
Discussion

The main finding of this study was that MetS was an independent predictor for 12-month MACE and TVR in the high LDL-C population, although it was not an independent predictor in the overall population. There were no significant differences in the incidences of cardiac death and Non-fatal myocardial infarction between the MetS group and the Non-MetS group in the high LDL-C population.

There have been many studies that have reported an impact of MetS on cardiovascular morbidity and mortality in AMI patients, and there have been some disagreements formed. Some studies showed that MetS was associated with poor outcomes after AMI, including severe heart failure, by Zeller et al. and in-hospital death in patients with ST elevation myocardial infarction (STEMI), by Lee et al. Other studies, however, have found that MetS was not associated with poor outcomes after PCI. Kim et al. reported that MetS was not an independent predictor of increased in-stent restenosis and MACE in patients with angina and significant coronary artery stenosis, excluding STEMI. Hoffmann et al. also reported that MetS patients without diabetes did not have an increased risk for MACE during a 12-month follow-up period after stent placement. Rana et al. also showed that MetS was not associated with TVR after PCI in patients with stable angina, non-ST-elevation acute coronary syndromes, or silent ischemia with PCI. However, meta-analysis showed that MetS was associated with a significant increased risk of post-stent all-cause mortality and MACE in CAD patients with DES.

Our results in the overall population were consistent with previous studies by Kim et al. and Rana et al. However, our results in the high LDL-C population showed similar trends in results to the previous meta-analysis, although there are some differences. MetS in the high LDL-C population was associated with an increased risk of MACE and TVR in our study, while an increased risk of all-cause mortality and MACE in the meta-analysis. These discrepancies between meta-analysis findings and our study may be due to the dissimilarities in patient populations, which are differences in the species of stents, and follow-up periods. In addition, our study included diabetic patients, while other studies did not. Coming together with these earlier studies, our study might suggest that MetS could be an important risk factor in some populations of AMI patients.

There are possible mechanisms to explain how MetS could have an adverse influence on the clinical outcomes in AMI patients. First, there is a large difference in the dyslipidemia pattern between the MetS group and the Non-MetS group. The MetS group had atherogenic dyslipidemia, which consists of high triglyceride and lower HDL-C, as well as qualitative dyslipidemia, which consists of small dense LDL-C (sd-LDL-C) and lipoprotein (Lp) (a). Sd-LDL-C and Lp (a), rather than LDL-C, have been known to be major risk factors for atherogenic dyslipidemia as well as for the severity of CAD, which causes oxidative stress, endothelial dysfunction, and the inflammation of vessels.

Second, inflammation caused by obesity has been known to play an important role in the pathogenesis of MetS-associated re-stenosis by releasing inflammatory adipocytokines, such as leptin, tumor necrosis factor-α, plasminogen activator inhibitor-1, and interleukins 1 and 6. In the present study, hsCRP, a biomarker for inflam-
In AMI patients, regardless of LDL-C level, by recent guidelines. AMI patients in real-world clinical practice. Statin has been indicated more rapid and aggressive treatment should be given to those patients with atypical presentation or NSTEMI, should be made, and AMI patients, especially in patients with poor characteristics or in specialized long-term follow up studies are required in this area. Therefore, we suggest that statin treatment rates should be enhanced in AMI patients with MetS.

Finally, symptom to door time was longer in AMI patients with MetS than among those without MetS in the present study, which might negatively influence the clinical outcomes. What might be the reason for this? MetS patients had a higher prevalence of diabetes and were older. They were also more likely to be female. These factors could, in turn, have led to more atypical symptoms with a higher rate in MetS patients than in Non-MetS patients (13.4% vs. 11.1%, p=0.007, respectively). These factors might be related to delays in hospital visits, because it is not easy for most patients to recognize that atypical symptoms are associated with CAD. Therefore, we suggest that meticulous education in atypical symptoms, as a type of possible presentation of AMI, should be given to patients who are older or hypertensive or diabetic in outpatient clinics before the onset of AMI in addition to conventional treatment.

Our analysis faces several limitations. First, although these results come from a large cohort study, this was a multi-center trial and retrospective study, so there is the possibility of selection bias. Second, there are many missing data features, including fasting blood sugar, sd-LDL-C, Lp (a), and 12-month follow-up LDL level in our registry. Third, our data for blood pressure and blood glucose were checked at admission. The checked level of blood glucose (mean; 173.4±81.38 mg/dL) and blood pressure (mean; systolic 129.3±30.51 mg/dL) were higher than the usual condition because of the unstable and emergent condition. Thus, it seemed to be inappropriate to use those data points for the diagnosis of MetS. Our study might have overcome this limitation by involving patients with a known history of hypertension and diabetes instead of blood pressure and blood glucose. The present study might be a reference for MetS patients with AMI in the Korean population, because, to date, the data for MetS patients with AMI is relatively insufficient. More specialized long-term follow up studies are required in this area.

In conclusion, AMI patients with MetS had significantly worse clinical outcomes when compared with Non-MetS patients, in patients with higher LDL-C of more than 100 mg/dL, although those in the overall population showed no significant difference in 12-month clinical outcomes. Therefore, it is important to ascertain the presence of MetS in AMI patients, and provide more aggressive therapy, including the early initiation of PCI, as well as the greater use of GP2b3A inhibitors. Greater statin treatment should also be strongly considered.

Acknowledgments

This study was conducted with the support of the Korean Circulation Society in commemoration of its 50th Anniversary.
References

1. Skilton MR, Moulin P, Sérusclat A, Nony P, Bonnet F. A comparison of the NCEP-ATPIII, IDF and AHA/NHLBI metabolic syndrome definitions with relation to early carotid atherosclerosis in subjects with hypercholesterolemia or at risk of CVD: evidence for sex-specific differences. Atherosclerosis 2007;190:416-22.

2. Lorenzo C, Okoloise M, Williams K, Stern MP, Haffner SM; San Antonio Heart Study. The metabolic syndrome as predictor of type 2 diabetes: the San Antonio heart study. Diabetes Care 2003;26:3153-9.

3. Girman CJ, Rhodes T, Mercuri M, et al. The metabolic syndrome and risk of major coronary events in the Scandinavian Simvastatin Survival Study (4S) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). Am J Cardiol 2004;93:136-41.

4. Selcuk H, Temizhan A, Selcuk MT, et al. Impact of metabolic syndrome on future cardiovascular events in patients with first acute myocardial infarction. Coron Artery Dis 2009;20:370-5.

5. Karthikeyan G, Teo KK, Islam S, et al. Lipid profile, plasma apolipoproteins, and risk of a first myocardial infarction among Asians: an analysis from the INTERHEART Study. J Am Coll Cardiol 2009;53:244-53.

6. Sim DS, Jeong MH, Kang JC. Current management of acute myocardial infarction: experience from the Korea Acute Myocardial Infarction Registry. J Cardio 2010;56:1-7.

7. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005;112:2735-52.

8. Zeiler M, Steg PG, Ravisse J, et al. Prevalence and impact of metabolic syndrome on hospital outcomes in acute myocardial infarction. Arch Intern Med 2005;165:1192-8.

9. Lee MG, Jeong MH, Ahn Y, et al. Impact of the metabolic syndrome on the clinical outcome of patients with acute ST-elevation myocardial infarction. J Korean Med Sci 2010;25:1456-61.

10. Kim JS, Lee HC, Choi BK, et al. Impact of metabolic syndrome on in-stent restenosis and clinical outcomes after percutaneous coronary stent implantation. Diabetes Res Clin Pract 2010;88:e38-41.

11. Hoffmann R, Stellbrink E, Schröder J, et al. Impact of the metabolic syndrome on angiographic and clinical events after coronary intervention using bare-metal or sirolimus-eluting stents. Am J Cardiol 2007;100:1347-52.

12. Rana JS, Monraats PS, Zwinderman AH, et al. Metabolic syndrome and risk of restenosis in patients undergoing percutaneous coronary intervention. Diabetes Care 2005;28:873-7.

13. Xu D, Guo Y, Wang H, et al. The angiographic and clinical outcomes after coronary stenting in patients with metabolic syndrome. Atherosclerosis 2012;221:416-21.

14. Ascaso J, Gonzalez Santos P, Hernandez Mijares A, et al. Management of dyslipidemia in the metabolic syndrome: recommendations of the Spanish HDL-Forum. Am J Cardiovasc Drugs 2007;7:39-58.

15. Fukushima Y, Hirayama S, Ueno T, et al. Small dense LDL cholesterol is a robust therapeutic marker of statin treatment in patients with acute coronary syndrome and metabolic syndrome. Clin Chim Acta 2011;412:4123-7.

16. Koba S, Yokota Y, Hirano T, et al. Small LDL-cholesterol is superior to LDL-cholesterol for determining severe coronary atherosclerosis. J Atheroscler Thromb 2008;15:250-60.

17. Moon JY, Kwon HM, Kwon SW, et al. Lipoprotein(a) and LDL particle size are related to the severity of coronary artery disease. Cardiology 2007;108:282-9.

18. Yazdandoust S, Parizadeh SM, Moehebati M, et al. Serum small dense low-density lipoprotein concentrations are elevated in patients with significant coronary artery stenosis and are related to features of the metabolic syndrome. Lipids 2012;47:963-72.

19. Goswami B, Rajappa M, Singh B, Ray PC, Kumar S, Maillka V. Inflammation and dyslipidaemia: a possible interplay between established risk factors in North Indian males with coronary artery disease. Cardiovasc J Afr 2010;21:103-8.

20. Greenberg AS, Obin MS. Obesity and the role of adipose tissue in inflammation and metabolism. Am J Clin Nutr 2006;83:4615-55.

21. Goyal SN, Bhatti S, Krishnamurthy B, Agrawal Y, Ojha SK, Arya DS. Impact of metabolic syndrome on re-stenosis development: role of drug-eluting stents. Diob Vasc Dis Res 2012;9:177-88.

22. Deedwania PC, Hunninghake DB, Rays HE, et al. Effects of rosuvastatin, atorvastatin, simvastatin, and pravastatin on atherogenic dyslipidemia in patients with characteristics of the metabolic syndrome. Am J Cardiol 2005;95:380-6.

23. Baldassarre S, Scruel O, Deckelbaum RJ, Dupont IE, Ducobu J, Carpenti-er YA. Beneficial effects of atorvastatin on sd LDL and LDL phenotype B in statin-naive patients and patients previously treated with simvas- tin or pravastatin. Int J Cardiol 2005;104:338-45.

24. Bahadir MA, Ozug A, Uzunulu M, Bahadir O. Effects of different statin treatments on small dense low-density lipoprotein in patients with metabolic syndrome. J Atheroscle 2009;16:684-90.

25. Devaraj S, Chen E, Jialal I. Direct demonstration of an antiinflammatory effect of simvastatin in subjects with the metabolic syndrome. J Clin Endocrionol Metab 2006;91:4489-96.

26. Ray KK, Cannon CP. Intensive statin therapy in acute coronary syn- dromes: clinical benefits and vascular biology. Curr Opin Lipidol 2004;15:637-43.

27. Filardi PP, Cecere M, Savarese G, et al. Inflammation and lipids in the coronary pathology. Risk factors, causes or therapeutic target?. G Ital Cardiol (Rome) 2010;11(12 Suppl 3):105-55.

28. Ulus T, Parspour A, Cavusoglu Y, Entok E, Uslu I, Demirustu C. Statins improve myocardial perfusion in metabolic syndrome patients who have perfusion defects on myocardial perfusion imaging and angiographically normal coronary arteries. Eur Rev Med Pharmacol Sci 2012;16:328-34.

29. Murrow JR, Sher S, Ali S, et al. The differential effect of statins on oxidative stress and endothelial function: atorvastatin versus pravastatin. J Clin Lipidol 2012;6:42-9.

30. Task Force on the management of ST-segment elevation acute myo- cardiac infarction of the European Society of Cardiology (ESC), Steg PG, James SK, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur J Heart J 2012;33:2569-619.