Lipid-Lowering Treatment Practice Patterns in Korea: Comparison with the Data Obtained from the CEPHEUS Pan-Asian Study

Jidong Sung1, Sang Hyun Kim2, Hye Ryoung Song3,4, Myung Hwan Chi3 and Jeong Euy Park1

1 Division of Cardiology, Heart Vascular and Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
2 Division of Cardiology, Boramae Hospital, Seoul National University School of Medicine, Seoul, Korea
3 Medical Department, AstraZeneca Korea, Seoul, Korea
4 Graduate School of Public Health, Seoul National University, Seoul, Korea

Aim: The Pan-Asian CEPHEUS study assessed low-density lipoprotein cholesterol (LDL-C) goal attainment among patients under lipid-lowering therapy. We compared Korean and other Asian data in order to investigate international variations in clinical practice in the field of cardiology.

Methods: Hypercholesterolemic patients ≥18 years of age who had been on lipid-lowering treatment for ≥3 months were recruited from eight Asian countries. The lipid concentrations were measured, and demographic and other relevant data were collected. In addition, the cardiovascular risk was determined using criteria established in the updated 2004 NCEP guidelines.

Results: In Korea, 92 cardiologists enrolled 1,584 patients. The data of these patients were compared with those for 2,060 patients enrolled by 135 cardiologists from other Asian countries in the CEPHEUS study. The proportion of high-risk patients, frequency of use of more potent LDL-C-lowering regimens and rate of LDL-C goal attainment were significantly greater in the Korean subjects than those observed in the other Asian populations. In addition, the Korean patients were more likely to achieve the LDL-C target (odds ratio = 1.37, 95% confidence interval 1.11-1.70) after adjusting for the LDL-C target level, use of potent LDL-C-lowering regimens, the baseline LDL-C level, age and systolic blood pressure.

Conclusions: There was a significant difference in the goal attainment rate between Korea and the other Asian countries. Korean cardiologists appear to be relatively more aggressive with lipid-lowering treatment than other Asian cardiologists.


Key words: Hypercholesterolemia, Low-density lipoprotein cholesterol, Goal attainment, Cardiovascular risk

Introduction

Despite the availability of well-established and evidence-based treatment guidelines for the management of cardiovascular diseases, there are significant treatment gaps and regional variation in attainment of treatment goals designated in the appropriate guidelines1-7) and in practice patterns, including in the prescription of lipid lowering agents8-11).

Although various studies have previously addressed regional differences, few studies have so far been conducted regarding international differences in medical practice in the cardiovascular field12,13), with studies in Asian countries being even more rare. As variation in clinical practice may be related to differences in outcomes, differences in regional and/or international practice patterns and the possible underlying causes should be analyzed in order to improve the quality of care.
The current state of poor management of dyslipidemia has been well demonstrated by the findings of the CEntralized Pan-European survey on tHE Under-treatment of hypercholesterolemia (CEPHEUS) survey conducted in 2006 and 2007, which showed that 42.6% of patients receiving lipid-lowering drugs fail to attain their respective National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)-defined low-density lipoprotein cholesterol (LDL-C) goals. The CEPHEUS Pan-Asian study was carried out along the same lines as the European CEPHEUS study and showed wide inter-country variation in LDL-C goal achievement (according to the NCEP ATP III guidelines), ranging from 31.3% to 82.9% (31.3% to 52.7% after excluding the data for Hong Kong). However, making a direct comparison between Asian countries is difficult due to differences in the composition of the specialty of participating physicians, which varies widely from 100% cardiologists in South Korea to 95.5% primary care physicians in Malaysia.

The objective of this study was to investigate international differences in lipid-lowering treatment in Asian cardiology practice by comparing data for South Korea, which contributed the largest proportion of CEPHEUS Pan-Asian study subjects, with those of other participating countries.

Methods

The CEPHEUS Pan-Asian study (NCT00687492) was a prospective, multinational, cross-sectional survey of subjects under lipid-lowering pharmacological treatment. This multicenter survey was conducted at 405 sites in Korea, Taiwan, Thailand, Indonesia, Philippines, Malaysia, Vietnam and Hong Kong SAR, China, with a target enrolment of approximately 8,000 patients. The study protocol was reviewed and approved by the Investigational Review Board and Ethics Committee governing each participating center. A detailed description of the whole study population and survey methods has been previously published elsewhere.

Study Population

The study subjects included patients who fulfilled the following inclusion criteria: (i) 18 years of age or above, (ii) two or more cardiovascular risk factors as defined according to the updated 2004 NCEP ATP III guidelines and (iii) under treatment with lipid-lowering drugs for at least three months at the time of enrollment, with no dose changes for at least six weeks.

Survey Instrument and Procedure

The survey instrument consisted of one questionnaire each for the attending physician and patient, and a case record form for the physician to record the patient’s demographics, physical examination findings, cardiovascular medical history, known cardiovascular risk factors (including coronary heart disease or coronary heart disease risk equivalents and metabolic syndrome), past lipid profiles (if any), current lipid-lowering therapy and reason for treatment. The physician questionnaire comprised 23 questions designed to collect information on the physician’s characteristics. The patient questionnaire contained 17 questions designed to determine the patient’s perception of hypercholesterolemia and its management, his/her compliance with lipid-lowering treatment and personal satisfaction with the therapy.

The biochemical analyses were performed at local laboratories in the individual hospitals. The cardiovascular risk profile of each patient was determined based on criteria established according to the updated 2004 NCEP ATP III guidelines. Criteria for the ‘very high’ risk group (with an LDL-C goal of <70 mg/dL) were as follows: (i) diabetes and/or metabolic syndrome, (ii) history of acute coronary syndrome. Other possible criteria, such as ‘severe and poorly controlled risk factors,’ were not considered due to the difficulty in accurately classifying these characteristics.

Outcomes

The primary outcome of the study to compare the rate of LDL-C goal attainment with lipid-lowering treatment between the Korean and non-Korean groups. The secondary outcomes included a comparison of the LDL-C goal attainment rate between the Korean and non-Korean patients according to the risk level and predictors of LDL-C goal attainment.

Statistical Analysis

Descriptive statistics, including frequency distributions, medians, means and standard deviations, were used to describe the demographic data, anthropometric measurements, such as body weight, height and waist circumference, and concentrations of total cholesterol, LDL-C, high-density lipoprotein cholesterol and triglycerides in the Korean and non-Korean groups. In the analysis of the primary outcome variable, the percentage (with the 95% confidence interval (CI)) of patients achieving the LDL-C goals was determined and compared between the Korean and non-Korean patients according to the risk level and predictors of LDL-C goal attainment.
for multiple covariates, including variables determined to be significant predictors of LDL-C goal attainment based on previously published results\textsuperscript{15}). Due to the very high rate of goal attainment in Hong Kong compared with other countries in the CEPHEUS Pan-Asian study\textsuperscript{15}), all statistical analyses were performed excluding the Hong Kong data. Supplemental results including Hong Kong data are provided in Appendix 1. The SAS v9.1 for Windows software program (Cary, NC, USA) was used for the statistical analysis.

**Results**

Among the 7,281 subjects included in the CEPHEUS Pan-Asian study, 32 low-risk patients according to the NCEP ATP III risk stratification were excluded from the analysis in order to reduce confounding. Because all the Korean physicians involved in the study were cardiologists, compared with only 38.9% of the non-Korean physicians, the non-Korean patients treated in non-cardiology practices (n = 3,044) were also excluded from the analysis in order to compare the practice patterns of Korean and non-Korean cardiologists. Furthermore, the analysis excluded 561 patients of 13 cardiologists from the Hong Kong site, which was considered to be an outlier. The rationale for excluding the Hong Kong subjects is explained in the Discussion section. The final study population consisted of 1,584 Korean patients of 92 cardiologists and 2,060 patients of 135 cardiologists from other Asian countries (Fig. 1).

**Patient and Physician Characteristics**

The patient characteristics of the Korean and non-Korean groups are shown in Table 1. The Korean patients did not differ from the non-Korean patients in terms of age, gender proportion and smoking rate, although they exhibited a significantly lower prevalence of metabolic syndrome and were more likely to have coronary artery disease and be in the very high-risk group than the non-Korean patients (64.3% versus 54.1%, \( p < 0.0001 \)). Therefore, the LDL-C treatment goals differed between the Korean and non-Korean patient groups. However, the Korean patients had significantly lower body mass index and systolic and diastolic blood pressure values and a significantly reduced prevalence of diabetes compared with the non-Korean patients.

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**Fig. 1.** Study population (patients and physicians).
mon in the non-Korean patients (37.2% versus 45.4%, \(p<0.0001\)).

Some indicators of aggressive lipid-lowering treatment were observed more often in the Korean group. For example, statins were prescribed more frequently in the Korean than the non-Korean patients (96.9% versus 94%, \(p<0.0001\)), as was combination treatment (11.0% versus 9.0%, \(p<0.05\)) and potent LDL-C-lowering therapy (including atorvastatin, rosuvastatin and statin + ezetimibe) (45.4% versus 40.3%, \(p<0.01\)). However, the Korean practices enrolled more patients with coronary artery disease and those in the very high-risk stratification, versus the non-Korean practices. These characteristics may help to explain the more aggressive approach to lipid-lowering treatment noted among Korean cardiologists.

Table 1. Patient characteristics in the Korean and non-Korean groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Korean</th>
<th>Non-Korean</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1584</td>
<td>2060</td>
<td>0.542</td>
</tr>
<tr>
<td>Age of patients (years)</td>
<td>62.9 ± 9.9</td>
<td>63.1 ± 11.0</td>
<td>0.737</td>
</tr>
<tr>
<td>Proportion of male patients (%)</td>
<td>57.9</td>
<td>58.4</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.1 ± 3.1</td>
<td>25.7 ± 4.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>125.9 ± 14.8</td>
<td>133.8 ± 17.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>75.5 ± 10.0</td>
<td>79.6 ± 11.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

\(†\) Mean ± standard deviation.

Table 2. Comparison of lipid-lowering treatments between the Korean and non-Korean groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Korean</th>
<th>Non-Korean</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline LDL-C (mmol/L)</td>
<td>3.3 ± 1.1</td>
<td>3.8 ± 1.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Follow-up LDL-C (mmol/L)</td>
<td>2.2 ± 0.7</td>
<td>2.7 ± 1.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL-C reduction (%)</td>
<td>26.8</td>
<td>25.7</td>
<td>0.50</td>
</tr>
<tr>
<td>LDL-C reduction (mmol/L)</td>
<td>1.1 ± 1.1</td>
<td>1.2 ± 1.4</td>
<td>0.07</td>
</tr>
<tr>
<td>Duration of LLT (years)</td>
<td>2.6 ± 2.4</td>
<td>3.0 ± 3.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any treatment changes since initiation of LLT (%)</td>
<td>37.2</td>
<td>45.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Statin prescribed (%)</td>
<td>96.9</td>
<td>94.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Combination treatment (%)</td>
<td>11.0</td>
<td>9.0</td>
<td>0.04</td>
</tr>
<tr>
<td>Potent LDL-lowering regimen (%)</td>
<td>45.4</td>
<td>40.3</td>
<td>0.002</td>
</tr>
</tbody>
</table>

\(\dagger\) LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering treatment.  
\(\ddagger\) Including atorvastatin, rosuvastatin and statin + ezetimibe.
Patterns of Lipid-Lowering Treatment in Korea

Table 3. Unadjusted comparisons of the LDL-C goal attainment rates among the Korean and non-Korean patients, overall and according to the cardiovascular risk level (excluding the Hong Kong data)

<table>
<thead>
<tr>
<th>Risk strata</th>
<th>Korean</th>
<th>Non-Korean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total group</td>
<td>51.2 (48.7-53.7, 811/1,584)</td>
<td>43.2 (41.0-45.3, 889/2,060)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Very high</td>
<td>31.5 (28.7-34.5, 321/1,018)</td>
<td>24.4 (21.9-27.0, 271/1,113)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>High</td>
<td>79.1 (74.3-83.4, 258/326)</td>
<td>56.4 (52.3-60.4, 335/594)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Moderate</td>
<td>96.7 (93.5-98.6, 232/240)</td>
<td>80.2 (75.6-84.2, 282/353)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

% (95% confidence interval, target achieved/total number).

Table 4. Predictors of LDL-C goal attainment according to the univariate analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C goal (reference &lt; 70 mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100 mg/dL</td>
<td>5.11 (4.28-6.11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;130 mg/dL</td>
<td>18.22 (13.89-23.89)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Korean (reference: non-Korean)</td>
<td>1.34 (1.12-1.53)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Potent LDL-lowering regimen†</td>
<td>1.25 (1.08-1.45)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL-C reduction (mmol/L)</td>
<td>1.02 (1.02-1.03)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Baseline LDL-C (for 1 mmol/L increase)</td>
<td>0.69 (0.63-0.76)</td>
<td>0.003</td>
</tr>
<tr>
<td>Age (for 10 year increase)</td>
<td>1.05 (0.98-1.11)</td>
<td>0.17</td>
</tr>
<tr>
<td>Gender (reference: male)</td>
<td>1.13 (0.98-1.30)</td>
<td>0.08</td>
</tr>
<tr>
<td>Adherence§</td>
<td>0.70 (0.53-0.94)</td>
<td>0.02</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.64 (0.54-0.72)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>0.44 (0.38-0.51)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SBP (for 10 mmHg increase)</td>
<td>0.91 (0.87-0.94)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

Comparison of LDL-C Goal Attainment Rates
The results of the unadjusted comparison of the LDL-C goal attainment rates in the Korean and non-Korean patients are shown in Table 3. Overall, the Korean patients had a significantly higher LDL-C goal attainment rate than the non-Korean patients (51.2% versus 43.2%, p < 0.0001). The rate of LDL-C goal attainment was also significantly higher in the Korean than the non-Korean patients at all cardiovascular risk levels, from moderate to very high.

Predictors of LDL-C Goal Attainment
Table 4 shows the predictors of LDL-C goal attainment identified according to the univariate analysis. Positive predictors included a lower risk level (higher LDL-C treatment goal), a Korean (versus non-Korean) nationality, the use of potent LDL-C-lowering agents, including rosvastatin, atorvastatin and statin + ezetimibe, a greater LDL-C reduction and allegedly superior adherence on the patient questionnaire. Negative predictors were a high baseline LDL-C level, smoking, metabolic syndrome and high systolic blood pressure.

Table 5 summarizes the findings of a multivariable-adjusted logistic regression model conducted to determine whether the Korean patients were more likely to achieve their LDL-C goals than those from the other Asian countries. The Korean patients displayed an odds of 1.37 (95% CI 1.11-1.70) of attaining their LDL-C treatment target after adjusting for the LDL-C treatment goal, use of potent LDL-C-lowering agents, baseline LDL-C, age and systolic blood pressure. The alleged level of adherence to treatment and presence of metabolic syndrome were not found to be independent predictors of LDL-C goal attainment.

Discussion
In this study, the rate of LDL-C goal achievement in cardiology practice was significantly higher among South Korean patients than among those from
According to the findings of the present study, Korean cardiologists appear to be more aggressive in terms of prescribing lipid-lowering treatment than cardiologists from other Asian countries, with the possible exception of Hong Kong. Korean cardiologists more frequently use statins, combination regimens and potent LDL-C-lowering agents than other Asian cardiologists (Table 3). The Lipid Treatment Assessment Project 2 (LTAP 2) study included nine countries worldwide (US, Canada, France, the Netherlands, Spain, Brazil, Mexico, Korea and Taiwan), the results of which showed variation in the target LDL-C achievement rates, from 47% to 84%, across the participating countries. Korea was among the highest in terms of the LDL-C target attainment rate (83.5%) in that study. Although this finding is not directly comparable to the present results, as the above study did not take into consideration physician specialties or very high-risk patients, it is in accordance with our observation that Korean cardiologists are relatively aggressive in their use of lipid-lowering drugs.

It is unclear whether or why Korean cardiologists have a more aggressive attitude towards lipid-lowering therapy than those in most of the other countries included in the CEPHEUS Pan-Asian study. Possible explanations of the higher rates of LDL-C goal achievement in Korea include greater awareness of the importance of lipid-lowering treatment and/or more rapid acceptance of newer recommendations for treatment goals. The fact that the Korean cardiologists were seeing more patients with coronary artery disease and those in the very high-risk stratification group may also help to explain why these physicians possibly had a more aggressive attitude to lipid-lowering ther-

### Table 5. Multiple logistic regression model for predictors of LDL-C goal attainment

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korean (reference: non-Korean)</td>
<td>1.37 (1.11-1.70)</td>
<td>0.004</td>
</tr>
<tr>
<td>LDL-C goal (reference &lt;70 mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100 mg/dL</td>
<td>7.40 (5.76-9.50)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;130 mg/dL</td>
<td>28.38 (19.38-41.56)</td>
<td></td>
</tr>
<tr>
<td>Potent LDL-lowering regimen</td>
<td>1.76 (1.42-2.19)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Baseline LDL-C (for 1 mmol/L increase)</td>
<td>0.69 (0.63-0.76)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Age (for 10 year increase)</td>
<td>1.10 (1.00-1.21)</td>
<td>0.05</td>
</tr>
<tr>
<td>Adherence</td>
<td>0.84 (0.56-1.26)</td>
<td>0.39</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>0.88 (0.71-1.08)</td>
<td>0.22</td>
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<tr>
<td>SBP (for 10 mmHg increase)</td>
<td>0.93 (0.88-1.00)</td>
<td>0.04</td>
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OR, odds ratio; CI, confidence interval; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

† Potent LDL-lowering agents (rosuvastatin, atorvastatin or statin + ezetimibe) versus other regimens.

§ Patient always takes a tablet daily to lower cholesterol.

According to the findings of the present study, Korean cardiologists appear to be more aggressive in terms of prescribing lipid-lowering treatment than cardiologists from other Asian countries, with the possible exception of Hong Kong. Korean cardiologists more frequently use statins, combination regimens and potent LDL-C-lowering agents than other Asian cardiologists (Table 3). The Lipid Treatment Assessment Project 2 (LTAP 2) study included nine countries worldwide (US, Canada, France, the Netherlands, Spain, Brazil, Mexico, Korea and Taiwan), the results of which showed variation in the target LDL-C achievement rates, from 47% to 84%, across the participating countries. Korea was among the highest in terms of the LDL-C target attainment rate (83.5%) in that study. Although this finding is not directly comparable to the present results, as the above study did not take into consideration physician specialties or very high-risk patients, it is in accordance with our observation that Korean cardiologists are relatively aggressive in their use of lipid-lowering drugs.

Despite the availability of well-established and widely propagated treatment guidelines, there are significant treatment gaps and regional and international variation in the management of cardiovascular diseases. For example, studies in the US have documented significant regional and physician specialty-specific variation in lipid-lowering treatment. Previous studies have also addressed international variation in medical practice in terms of the prevalence, awareness and treatment of hypercholesterolemia. The European CEPHEUS study showed that the rate of LDL-C goal (according to the 2003 European Third Joint Task Force guidelines) attainment varies from 40% to 68% among the European countries participating in that study.

However, less is known about the degree of international variation in medical practice among Asian countries. The CEPHEUS Pan-Asian Study showed wide variation in the rate of LDL-C goal (NCEP ATP III guidelines) attainment, ranging from 31.3% to 82.9% (31.3% to 52.7% after excluding the Hong Kong data). The results also showed significant variation in the performance of different lipid-lowering regimens.

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<td>SBP (for 10 mmHg increase)</td>
<td>0.93 (0.88-1.00)</td>
<td>0.04</td>
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OR, odds ratio; CI, confidence interval; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

† Potent LDL-lowering agents (rosuvastatin, atorvastatin or statin + ezetimibe) versus other regimens.

§ Patient always takes a tablet daily to lower cholesterol.

other Asian countries after adjusting for covariates, including baseline the LDL-C level and LDL-C treatment goal. Although the population of the CEPHEUS Pan-Asian Study was not completely representative of patients encountered in Asian medical practice, as it did not include various major Far East Asian countries, such as Japan and China, or Middle and Southwest Asian countries, this analysis showed significant differences in cardiology practice between South Korea, a Far East Asian country, and Southeast Asian countries.

Despite the availability of well-established and widely propagated treatment guidelines, there are significant treatment gaps and regional and international variation in the management of cardiovascular diseases. For example, studies in the US have documented significant regional and physician specialty-specific variation in lipid-lowering treatment. Previous studies have also addressed international variation in medical practice in terms of the prevalence, awareness and treatment of hypercholesterolemia. The European CEPHEUS study showed that the rate of LDL-C goal (according to the 2003 European Third Joint Task Force guidelines) attainment varies from 40% to 68% among the European countries participating in that study.

However, less is known about the degree of international variation in medical practice among Asian countries. The CEPHEUS Pan-Asian Study showed wide variation in the rate of LDL-C goal (NCEP ATP III guidelines) attainment, ranging from 31.3% to 82.9% (31.3% to 52.7% after excluding the Hong Kong data). The results also showed significant variation in the performance of different lipid-lowering regimens.
apy than their non-Korean counterparts. Confirming this phenomenon likely requires a qualitative study, including techniques such as in-depth interviews with cardiologists, which is beyond the scope of this analysis.

However, the greater rate of LDL-C goal attainment may simply be due to lower baseline LDL-C levels in the Korean patients, the reasons for which are unclear. While the final lipid profiles were available for most of the patients in our analysis, a significant proportion of baseline LDL-C values were missing. For example, 20.5% (325/1,584) of the Korean patients did not have data for a recorded LDL-C level prior to treatment. Whether a low LDL-C level is a true characteristic of the Korean patient group or simply a chance phenomenon could not be determined based on the available data. It is rather paradoxical that the rate of reduction in LDL-C was not significantly different between the Korean and non-Korean patients despite the higher use of potent LDL-C lowering regimens and combination treatment in the Korean group. This finding may be due to the fact that the difference between the treatment regimens was moderate (Table 3). Although the resulting reduction in LDL-C did not differ significantly, the tendency to use a more potent lipid-lowering regimen despite a lower baseline LDL-C level may, after all, be suggestive of a more aggressive treatment policy among Korean cardiologists.

Although the Korean patients apparently had fewer risk factors, including lower baseline LDL-C levels, some of these features may not truly represent the general characteristics of Korean patients with coronary artery disease. For example, because this study did not exclude subjects who were already under pharmacological treatment, a significant number of patients were medicated at baseline, likely more strictly among the Korean patients. However, we do not have a definitive explanation for the lower prevalence of metabolic syndrome and obesity in the Korean group.

The primary finding of the CEPHEUS Pan-Asian study was that Hong Kong has a very high LDL-C target attainment rate (82.9%). The hospital that provided the Hong Kong data is a specialist center for cardiology, with policies that strictly adhere to international guidelines for cardiovascular disease prevention and an aggressive management strategy for patients with dyslipidemia, including up titration of the drug dose when necessary. This may explain the high rate of LDL-C goal achievement observed at this hospital compared with that observed in Korea and the other countries included in the CEPHEUS Pan-Asian study.

When the Hong Kong data were included in the comparison of Korean patients versus non-Korean patients, no significant differences were detected in the rate of LDL-C goal attainment due to the very high level of goal attainment among the very-high-risk Hong Kong patients (Appendix 1). This was true despite the significantly higher LDL-C goal attainment rates noted among the high- and moderate-risk Korean patients. We decided to exclude the Hong Kong data from the final analysis in the present study, as they may not be representative of overall cardiology practice in Hong Kong. For example, a study conducted at two other public hospitals in Hong Kong reported a lipid goal of 44% compared with 82.9% at the CEPHEUS study center. Furthermore, the data represent an outlier with a significant confounding effect on the comparison between South Korea and other Asian countries.

Both the European and Pan-Asian CEPHEUS studies reported the level of patient adherence to treatment and presence of metabolic syndrome to be significant predictors of LDL-C goal attainment. In this study, both of these factors were identified to be significant in the univariate analysis, although they did not independently predict LDL-C goal attainment in the multivariate analysis. This difference may be due differences in the physician specialties, in which 100% of physicians were cardiologists in this Korean study. Moreover, the alleged level of patient adherence may be a less important when physicians have a more aggressive attitude towards lipid-lowering and tend to prescribe potent LDL-C-lowering agents. Furthermore, why metabolic syndrome was found to be a negative predictor in previous studies is not clear, as it was not identified to be a significant factor in the present study after adjusting for the risk level. Therefore, the presence of metabolic syndrome may simply reflect a higher risk level.

Treatment guidelines have an important effect on clinical decisions. For example, a previous analysis of the CEPHEUS Asian data described the rate of use of guidelines among physicians. The majority (83.6%) of physicians used the NCEP ATP III guidelines, while the rate of use of European and/or local guidelines was much lower. However, the respondents stated that they referred to multiple guidelines when making clinical decisions; therefore, it is difficult to analyze the effects of any one specific set of treatment guidelines in a given country. However, the NCEP ATP III apparently had the greatest influence in most countries.

Limitations of the study include the fact that the findings cannot be directly extrapolated to other Far
East Asian countries, such as China and Japan, or other Korean physicians who are not cardiologists. In addition, as mainly Southeast Asian countries other than Korea were included in this study, the findings may not be extrapolated to other Asian countries. Finally, due to limitations in the sample size and sampling method, the study population may not represent the practice patterns observed throughout each country.

In conclusion, there was a significant difference in the rate of LDL-C goal attainment between Korea and other Asian countries in the CEPHEUS Pan-Asian study (excluding Hong Kong). Korean cardiologists appear to be relatively more aggressive in their use of lipid-lowering agents compared with cardiologists in other Asian countries.

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Conflicts of Interest

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References

Appendix 1. LDL-C goal attainment rate in Korean and non-Korean patients according to the risk levels (including Hong Kong data)

<table>
<thead>
<tr>
<th>Risk strata</th>
<th>Korean</th>
<th>Non-Korean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total group</td>
<td>51.2 (811/1,584)</td>
<td>50.0 (1,255/2,510)</td>
<td>NS</td>
</tr>
<tr>
<td>Very high</td>
<td>31.5 (321/1,018)</td>
<td>40.3 (622/1,542)</td>
<td>0.0002</td>
</tr>
<tr>
<td>High</td>
<td>79.1 (258/326)</td>
<td>57.1 (345/604)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Moderate</td>
<td>96.7 (232/240)</td>
<td>79.1 (288/364)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

% (target achieved/total number)