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Status of Lipid-Lowering Therapy Prescribed Based on Recommendations in the 2002 Report of the Japan Atherosclerosis Society Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese Adults: A Study of the Japan Lipid Assessment Program (J-LAP)

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ABSTRACT

Background: In its 1997 Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese Adults and subsequent revisions, the Japan Atherosclerosis Society (JAS) recommends serum lipid management goals (SLMGs) based on a coronary heart disease (CHD) risk classification. A literature search revealed that the status of lipid-lowering therapy based on the current JAS recommendations in Japan has not been assessed.

Objective: The aim of this study was to evaluate the efficacy of current lipid-lowering regimens, and to provide the best possible therapeutic strategies for patients with hyperlipidemia by identifying risk factors for the development of CHD, based on the current JAS recommendations.

Methods: This multicenter, retrospective study was conducted using data from patients under the care of physicians at 12,500 randomly selected institutions across Japan. Physicians received a survey concerning lipid-lowering therapy, on which each physician provided data from 10 consecutive adult patients with hyperlipidemia who had been prescribed lipid-lowering therapy for at least 3 months before the survey was administered, and who were undergoing routine follow-up on an outpatient basis. Physicians provided patients' demographic and clinical data, including JAS-defined CHD risk classification, coronary risk factors and pre- and posttreatment (after ≥3 months) serum lipid levels, and the types and dosages of drugs in patients' current and prior treatment regimens. These data were used to assess the efficacy of lipid-lowering regimens and rates of patients achieving the SLMGs recommended by the JAS.

*The J-LAP Investigators included 2540 physicians from 12,500 institutions across Japan.

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Results: A total of 2540 physicians participated in the survey, and data from 24,893 Japanese patients (mean [SD] age, 65.8 [10.5] years) with hyperlipidemia were included in the study. Patients with familial hyperlipidemia (845/24,893 [3.4%]) were excluded from most of the analyses, leaving 24,048 patients with primary hyperlipidemia. The most prevalent coronary risk factors included age (21,902 [91.1%]), hypertension (14,275 [59.4%]), diabetes mellitus type 2 and/or impaired glucose tolerance (6346 [26.4%]), and smoking (3841 [16.0%]). A total of 20,948 patients (87.1%) had a CHD risk classification of B (ie, ≥1 coronary risk factor but no history of CHD). At the time of the survey, the lipid-lowering regimens of 22,080 patients (91.8%) included a statin. The rates of achievement of SLMGs were as follows: total cholesterol (TC), 12,659/23,840 patients (53.1%); low-density lipoprotein cholesterol (LDL-C), 14,025/22,121 (63.4%); high-density lipoprotein cholesterol, 19,702/21,279 (92.6%); and triglycerides (TG), 14,892/23,569 (63.2%). TC and LDL-C goals were achieved by most patients (≥61.1%) in risk categories A, B1, and B2 (ie, 0–2 coronary risk factors; low to moderate risk) but by a low percentage of patients (≤45.4%) in risk categories B3, B4, and C (ie, ≥3 coronary risk factors or history of CHD; high risk). In the high-risk group (n = 10,515), the TC goal was achieved by 4059 patients (38.6%). The TC and LDL-C goals were achieved by significantly higher percentages of patients prescribed atorvastatin (5133/7928 [64.7%] and 5487/7426 [73.9%], respectively) compared with the rates of patients prescribed any other statin at the recommended starting doses (all, $P < 0.05$).

Conclusions: The results of this study of Japanese patients undergoing lipid-lowering therapy for the prevention of CHD, prescribed based on the recommendations in the JAS guideline, suggest insufficient reduction of TC, LDL-C, and TG in patients at high risk for CHD and the need for more aggressive lipid-lowering therapy in such patients. (*Curr Ther Res Clin Exp.* 2005;66:80–95)

Key words: J-LAP, hyperlipidemia, lipid-lowering therapy, guidelines, achievement rates for management goals, HMG-CoA reductase inhibitors, statins.

INTRODUCTION

Important risk factors for coronary heart disease (CHD) include hypercholesterolemia (total cholesterol [TC], ≥220 mg/dL; low-density lipoprotein cholesterol [LDL-C], ≥140 mg/dL), hypertension (systolic blood pressure/diastolic blood pressure, ≥160/≥95 mm Hg), age (men, ≥45 years; women, ≥55 years), diabetes mellitus type 2 (DM-2) (fasting plasma glucose level, ≥126 mg/dL) and/or impaired glucose tolerance (IGT) (plasma glucose level on glucose tolerance test, ≥140 and <200 mg/dL), smoking, a family history of CHD, depressed serum high-density lipoprotein cholesterol (HDL-C) (<40 mg/dL), obesity (body mass index, ≥25 kg/m^2), a history of cerebral infarction or arteriosclerosis obliterans (ASO), and a history of CHD. Major epidemiologic studies have established a statistical correlation between hypercholesterolemia and increased risk for CHD.[1,2]

The correlation between hypercholesterolemia and risk for CHD has also been demonstrated by the finding that decreased levels of serum TC and LDL-C lead to CHD risk reduction.[3,4]

The Japan Lipid Intervention Trial (J-LIT)[5] studied a cohort of >50,000 patients with hypercholesterolemia prescribed lipid-lowering therapy with simvastatin, a hydroxymethylglutaryl coenzyme A reductase inhibitor (statin), for 6 years (mean) for the primary prevention of CHD. J-LIT found a higher CHD risk when the mean TC concentration was ≥240 mg/dL and the mean LDL-C concentration was ≥160 mg/dL.[5,6] Based on the findings in J-LIT, the Japan Atherosclerosis Society (JAS) revised its Guideline for Diagnosis and Treatment of hyperlipidemia in Japanese Adults,[7,8] and in 2004 proposed the following CHD risk categories based on the number of CHD risk factors present, as follows: 0 risk factors, category A; 1, 2, 3, or ≥4 risk factors, category B1, B2, B3, or B4, respectively; and history of CHD, category C (**Table I**).[9] Categories A to B2 are considered low to moderate risk; categories B3 to C are considered high risk. The guideline also proposes a strict regimen to achieve serum lipid management goals (SLMGs) in patients at high risk.

Despite the JAS recommendations, in Japan there is insufficient consensus among physicians as to the choice of first-line therapy in patients with hyperlipidemia. A study undertaken based on the 1997 guideline[7] found that conventional therapy using lipid-lowering drugs resulted in insufficient achievements of SLMGs.[10] However, the guideline revisions[8,9] added a more intensive therapeutic strategy for the prevention of CHD in patients with hyperlipidemia and multiple risk factors, and has been accepted by general practitioners, but to date no studies of lipid-lowering therapy based on the revisions have been conducted. This study aimed to evaluate the efficacy of current lipid-lowering regimens, and to provide the best possible therapeutic strategies for patients with hyperlipidemia by identifying risk factors for the development of CHD, based on the current JAS recommendations.

MATERIALS AND METHODS

Survey Participants

This multicenter, retrospective study was conducted using data from patients under the care of physicians at 12,500 randomly selected centers across Japan. Between January and April 2003, physicians were sent an invitation to participate in a survey concerning lipid-lowering therapy. Physicians who returned the invitation were sent the survey by mail.

Study Population

Each physician recruited 10 consecutive patients aged ≥18 years with hyperlipidemia (TC, ≥220 mg/dL; triglycerides [TG], ≥150 mg/dL) who were prescribed lipid-lowering therapy for at least 3 months before the survey was administered, and who were undergoing routine follow-up on an outpatient basis.

Table I. Coronary Heart Disease Risk Classification in the Japan Atherosclerosis Society Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese Adults.

Category	Coronary Risk Factors*	SLMG, mg/dL				Management of Other Coronary Risk Factors		
		TC	LDL-C	HDL-C	TG	Hypertension	DM-2	Smoking
A	0	<240	<160	≥40	<150	Follow the guidelines of the Japanese Society of Hypertension	Follow the guidelines of the Japan Diabetes Society	Smoking cessation
B1	1	<220	<140					
B2	2							
B3†	3	<200	<120					
B4‡	≥4							
C	History of CHD§	<180	<100					

SLMG = serum lipid management goal; TC = total cholesterol; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; TG = triglycerides; DM-2 = diabetes mellitus type 2; CHD = coronary heart disease.
*Includes risk factors other than elevated LDL-C level: age (men, ≥45 years; women, ≥55 years), hypertension, DM-2 and/or impaired glucose tolerance (IGT), smoking, family history of CHD, depressed HDL-C level, obesity, history of CHD.
†DM-2 and/or IGT is regarded as B3 risk equivalent.
‡Cerebral infarction and/or arteriosclerosis obliterans is regarded as B4 risk equivalent.
§Myocardial infarction and/or symptomatic angina pectoris.
Adapted with permission.[8]

Patient data were excluded from the study if patients had a history of severe traumatic injury, severe infectious disease, or major surgery within 12 months before the survey was administered.

Methods

Data from a subgroup of patients who were switched to a statin from another drug, including a statin differing from the one originally prescribed, were analyzed to determine the effects of statins as second-line therapy. Because the Third Report of the National Cholesterol Educational Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (NCEP ATP III)[11] indicates that patients with familial hyperlipidemia (FH) are resistant to the effects of most cholesterol-lowering medications, including statins, due to a lack of LDL-receptor activity,[11] patients with FH were included in a separate subanalysis.

Physicians provided patients' demographic and clinical data, including coronary risk factors, from patients' files. Patients were assigned a CHD risk category based on the JAS recommendations (**Table I**), which defines patients with hyperlipidemia but no history of CHD and no coronary risk factors as category A, and those with no history of CHD but ≥1 other risk factor, not including elevated LDL-C level, as category B. Category B is subcategorized as B1 to B4, corresponding to the number of coronary risk factors present. Patients with DM-2 and/or IGT are categorized as B3 risk equivalent, even if no other risk factors are present (similar to the CHD risk in the NCEP ATP III[11]). Patients with a history of cerebral infarction or ASO are categorized as B4 or C risk equivalent. Those with a history of CHD are classified as category C for secondary prevention. Similar to the NCEP ATP III,[11] the JAS guideline uses CHD risk classification, as well as serum lipid levels, to determine therapy intensity.

Data regarding the types and dosages of patients' current lipid-lowering regimens, as well as regimens prescribed just before the current one, if any, were also collected. Patients' current serum lipid levels and those measured just before the switch to the current regimen, if any, were noted. LDL-C was calculated using the Friedewald formula,[12] as follows:

$$\text{LDL-C} = \text{TC} - \text{HDL-C} - (\text{TG}/5),$$

where TG is the serum triglyceride level. When this formula could not be applied due to missing data, we used LDL-C levels from direct homogeneous assay.

Statistical Analysis

The significance of multiple pairwise comparisons was determined using the Student's *t* test. A P value <0.05 was considered statistically significant. Data are expressed as mean (SD).

RESULTS

Study Population

Demographic and Clinical Characteristics

Data from 25,261 patients were collected from 2540 physicians across Japan. Data from 368 of these patients were excluded for various reasons (eg, data concerning drug prescribed, lipid levels unavailable), bringing the number of study patients to 24,893 (17,184 women, 7709 men; mean [SD] age, 65.8 [10.5] years; mean [SD] height, 155.3 [8.8] cm; mean [SD] body weight, 58.6 [10.9] kg; mean [SD] body mass index, 24.2 [3.4] kg/m^2). Eight hundred forty-five patients (3.4%; 584 women, 261 men) had FH.

Coronary Risk Factors and Risk Classification

Figure 1 shows the prevalence of coronary risk factors in the 24,048 patients with primary hyperlipidemia. The most prevalent risk factor was age (21,902 patients [91.1%]), followed by hypertension (14,275 [59.4%]), DM-2 and/or IGT (6346 [26.4%]), smoking (3841 [16.0%]), history of CHD (2319 [9.6%]), and depressed HDL-C level (2196 [9.1%]).

When the 24,048 patients with primary hyperlipidemia were classified based on coronary risk factors according to the JAS 2002 guideline,[8] 781 (3.2%) were classified as category A, 5419 (22.5%) as B1, 7219 (30.0%) as B2, 5667 (23.6%) as B3, 2643 (11.0%) as B4, and 2319 (9.6%) as C. Thus, 20,948 patients (87.1%) were classified as category B, 18,305 (87.4%) of whom were classified as B1 to B3 (**Figure 2**).

Of the patients in category B3 (n = 5667), 1696 (29.9%) had 3 coronary risk factors other than DM-2 and/or IGT, and 3971 (70.1%) had DM-2 and/or IGT (ie, B3 risk equivalent). Of the patients in category B4 (n = 2643), 1132 (42.8%) had 3 or 4 risk factors plus DM-2 and/or IGT, 897 (33.9%) had a history of cerebral infarction or ASO (ie, B4 risk equivalent), 474 (17.9%) had DM-2 and/or IGT in addition to a history of cerebral infarction or ASO, and 235 (8.9%) had ≥4 risk factors other than DM-2 and/or IGT.

Therapy Prescribed

At the time of the survey, 22,080 patients (91.8%) were prescribed a combination therapy regimen that included a statin. Of these, 21,138 (95.7%) were prescribed statin monotherapy. Of these 21,138 patients, 7996 (37.8%) were prescribed atorvastatin, 7592 (35.9%) pravastatin, 3536 (16.7%) simvastatin, and 2014 (9.5%) fluvastatin. A total of 21,221 of these 22,080 patients (96.1%) were prescribed the starting dose of these drugs, as follows: atorvastatin 10 mg/d (7852 patients [37.0%]), pravastatin 10 mg/d (7640 [36.0%]), simvastatin 5 mg/d (3607 [17.0%]), and fluvastatin 20 mg/d (2122 [10.0%]). Only 740 patients (3.5%) were prescribed an up-titrated dose of a statin (data not shown).

Serum Lipid Levels

Mean (SD) serum lipid levels after ≥3 months of treatment in the patients with primary hyperlipidemia (n = 24,048) were as follows: TC, 208.6 (31.3) mg/dL

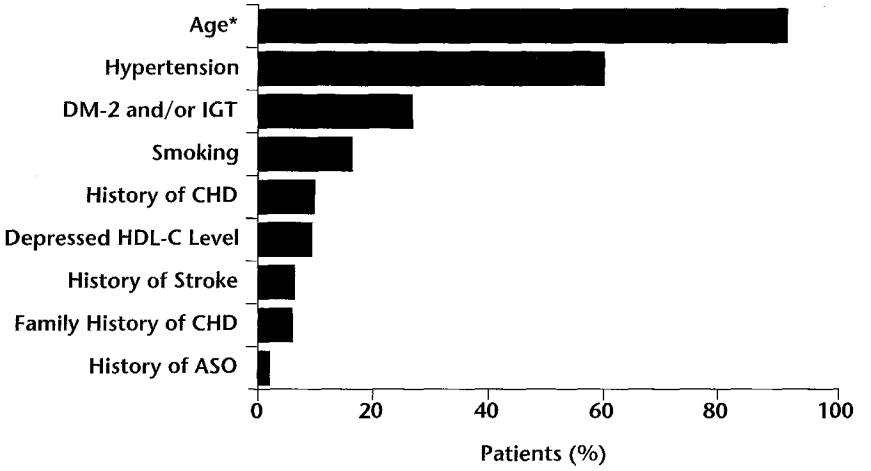

Figure 1. Distribution of study patients across coronary risk factors (n = 24,048; data from patients with familial hyperlipidemia are not included). DM-2 = diabetes mellitus type 2; IGT = impaired glucose tolerance; CHD = coronary heart disease; HDL-C = high-density lipoprotein cholesterol; ASO = arteriosclerosis obliterans. *Men, ≥45 years; women, ≥55 years.

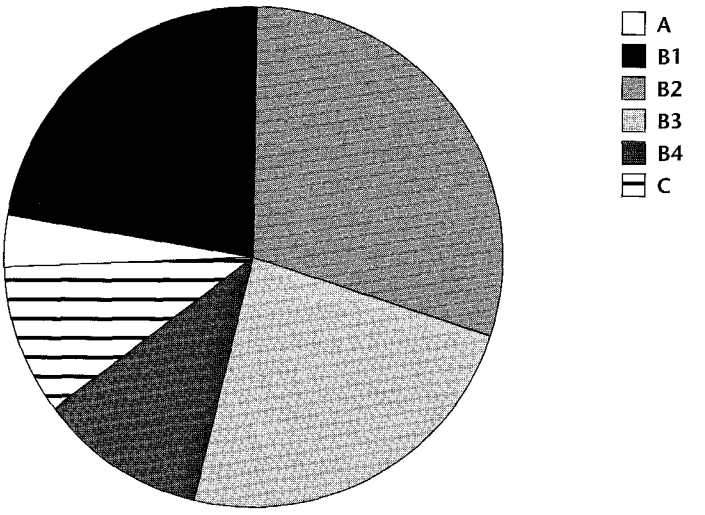

Figure 2. Distribution of study patients across coronary heart disease risk categories defined in a revision of the Japan Atherosclerosis Society Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese Adults[9] (n = 24,048; data from patients with familial hyperlipidemia are not included). See **Table I** for definitions of risk categories.

(n = 23,840); LDL-C, 122.1 (37.1) mg/dL (n = 22,121); HDL-C, 59.4 (17.2) mg/dL (n = 21,279); and TG, 147.8 (97.4) mg/dL (n = 23,569). The rates of achievement of SLMGs were as follows: TC, 12,659/23,840 patients (53.1%); LDL-C, 14,025/22,121 (63.4%); HDL-C, 19,702/21,279 (92.6%); and TG, 14,892/23,569 (63.2%). When serum levels of TC (**Figure 3A**) and LDL-C (**Figure 3B**) were distributed by CHD risk category, they were nearly identical.

Efficacy of Starting Doses of Statins Used as Second-Line Therapy

Of 7102 patients prescribed a statin as second-line therapy, 1044 (14.7%) were switched from a previous therapy not containing a statin, 5965 (84.0%) from another statin, 672 (9.5%) from a fibrate, 372 (5.2%) from other drugs, and 93 (1.3%) from unknown drugs.

The effects of second-line treatment with a statin at the starting dose on serum lipid levels and the rates of achieving SLMGs with this drug class are shown in **Table II**. Treatment with atorvastatin or simvastatin was associated with significant reductions in mean serum TC, LDL-C, and TG levels (changes, –19.3%, –27.5%, and –18.7%, respectively) (all, $P < 0.05$). The rates of achieving TC and LDL-C goals were significantly greater with atorvastatin (2571/4167 [61.7%] and 2586/3586 [72.1%], respectively) compared with simvastatin (309/682 [45.3%] and 339/575 [59.0%], respectively) (both, $P < 0.05$). The 7102 patients prescribed a statin as second-line therapy experienced significant decreases in TC, LDL-C, and TG (changes, –14.7%, –21.0%, and –17.5%, respectively) (all, $P < 0.05$) and a significant increase in HDL-C (1.0%; $P < 0.05$). Moreover, the rates of achieving SLMGs significantly increased after the prescription change for TC (from 17.4% to 54.5%), LDL-C (from 27.2% to 65.0%), and TG (from 50.3% to 61.6%) (all, $P < 0.05$) (data not shown).

TC goals were achieved in 541/706 patients (76.6%) in category A, 3040/4944 (61.5%) in B1, 4232/6380 (66.3%) in B2, 1957/4803 (40.7%) in B3, 972/2132 (45.6%) in B4, and 544/1985 (27.4%) in C. LDL-C goals were achieved by 600/688 (87.2%) of patients in category A, 3485/4669 (74.6%) in B1, 4639/5964 (77.8%) in B2, 2283/4441 (51.4%) in B3, 1059/1950 (54.3%) in B4, and 559/1814 (30.8%) in C.

The rates of achieving TC and LDL-C goals were significantly higher in patients prescribed atorvastatin (5133/7928 patients [64.7%] and 5487/7426 patients [73.9%], respectively) compared with simvastatin (1788/3490 [51.2%] and 2072/3277 [63.2%], respectively), fluvastatin (954/2002 [47.7%] and 1081/1855 [58.3%], respectively), and pravastatin (3411/7530 [45.3%] and 3985/6968 [57.2%], respectively) (all, $P < 0.05$) (**Figure 4**).

When rates of achievement of TC (**Figure 5A**) and LDL-C (**Figure 5B**) goals were distributed by CHD risk category, patients who were prescribed atorvastatin had the highest rates (TC, 5133/7928 patients [64.7%]; LDL-C, 5487/7426 [73.9%]). The mean rate of achieving the HDL-C goals by statins across risk categories was 92.6%; the mean rate of achieving the TG goals by statins across all risk categories was 63.2% (data not shown).

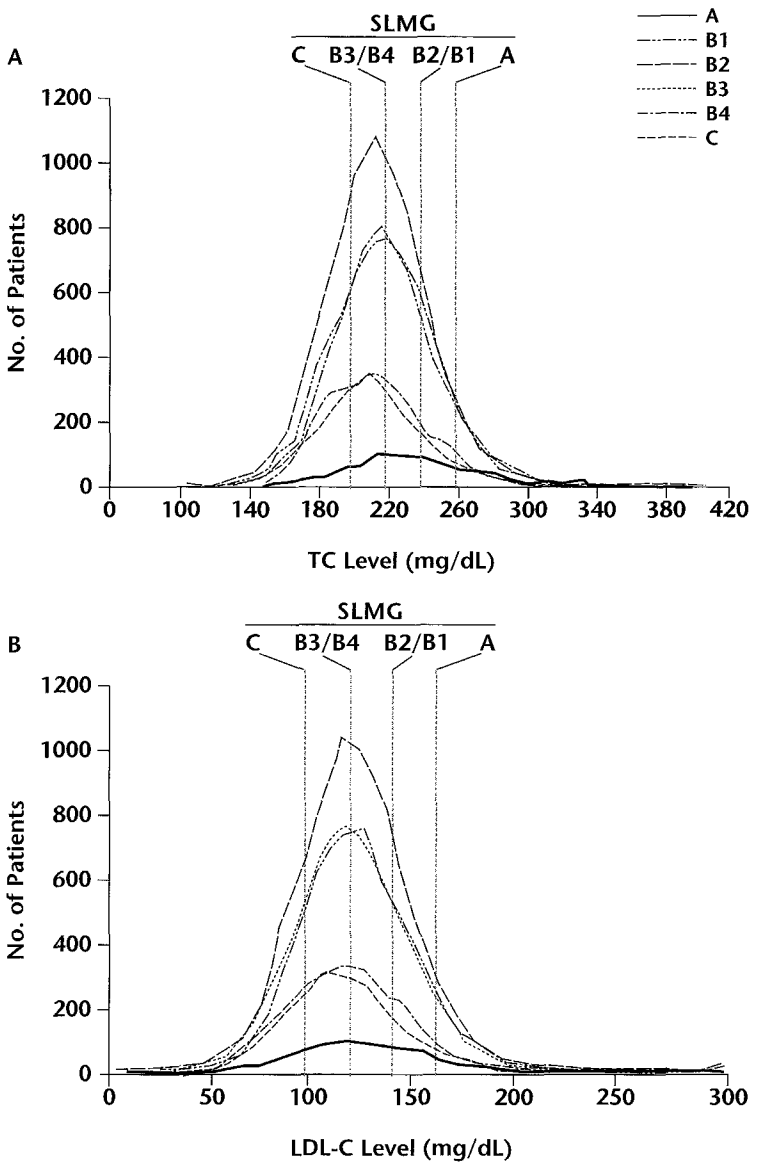

Figure 3. Distribution of serum levels of total cholesterol (TC) (A) and low-density lipoprotein cholesterol (LDL-C) (B) by coronary heart disease (CHD) risk category in patients with hyperlipidemia prescribed lipid-lowering therapy based on recommendations in a revision of the Japan Atherosclerosis Society (JAS) Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese Adults[9] (TC, n = 23,840; LDL-C, n = 22,121). The serum lipid management goal (SLMG) for each CHD risk category as recommended by the JAS is shown. See **Table I** for definitions of CHD risk categories.

Table II. Serum lipid concentrations and achievement rates of serum lipid management goals (SLMGs)* before and after ≥3 months of second-line lipid-lowering treatment with a hydroxymethylglutaryl coenzyme A reductase inhibitor (statin) at the starting dose in patients with primary hyperlipidemia (n = 22,080).

Statin/Lipid	No. of Patients	Serum Lipid Concentration, Mean (SD), mg/dL		SLMG Achievement Rate, No. (%)	
		Before	After	Before	After
Atorvastatin					
TC	4167	251.4 (35.1)	202.8 (32.0)†	429 (10.3)	2571 (61.7)‡
LDL-C	3586	158.8 (42.9)	115.2 (33.3)†	746 (20.8)	2586 (72.1)‡
TG	4035	183.1 (130.1)	148.9 (89.6)†§	1941 (48.1)	2498 (61.9)
Pravastatin					
TC	923	229.2 (40.1)	215.3 (29.3)†	289 (31.3)	395 (42.8)
LDL-C	770	142.4 (42.6)	128.9 (29.2)†	305 (39.6)	412 (53.5)
TG	892	156.2 (121.8)	150.0 (111.8)	553 (62.0)	553 (62.0)
Simvastatin					
TC	682	238.5 (36.4)	213.6 (29.6)†	137 (20.1)	309 (45.3)
LDL-C	575	149.1 (35.5)	125.3 (27.2)†	170 (29.6)	339 (59.0)
TG	659	165.1 (132.4)	147.9 (91.5)†§	394 (59.8)	408 (61.9)
Fluvastatin					
TC	464	231.9 (36.1)	217.7 (28.4)†	118 (25.4)	190 (41.0)
LDL-C	393	143.7 (34.4)	131.2 (39.5)†	135 (34.4)	199 (50.6)
TG	449	150.1 (80.7)	144.4 (93.7)	262 (58.4)	285 (63.5)

TC = total cholesterol; LDL-C = low-density lipoprotein cholesterol; TG = triglycerides.
*See **Table I** for SLMGs.
†$P < 0.05$ versus before treatment.
‡$P < 0.05$ versus simvastatin.
§$P < 0.05$ versus pravastatin and fluvastatin.

Therapies Administered to Patients with Familial Hyperlipidemia

Of the 845 patients (3.4%) with FH, 693 (82.0%) were prescribed monotherapy with a statin. Of those patients, 344 (49.6%) were prescribed atorvastatin, 183 (26.4%) pravastatin, 107 (15.4%) simvastatin, and 59 (8.5%) fluvastatin. The majority of patients (9723 [40.4%]) were prescribed the starting dose of the statin, although 686 (2.9%) were prescribed a higher dose. Mean (SD) serum lipid levels posttreatment in the patients with FH were as follows: TC, 227.2 (40.3) mg/dL (n = 833); LDL-C, 140.1 (59.1) mg/dL (n = 776); HDL-C, 58.6 (17.0) mg/dL (n = 768); and TG, 160.0 (143.3) mg/dL (n = 832). Using category C SLMGs, the TC goal was achieved by 72/833 patients (8.6%), LDL-C by 102/776 (13.1%), HDL-C by 700/768 (91.1%), and TG by 508/832 (61.1%) (data not shown).

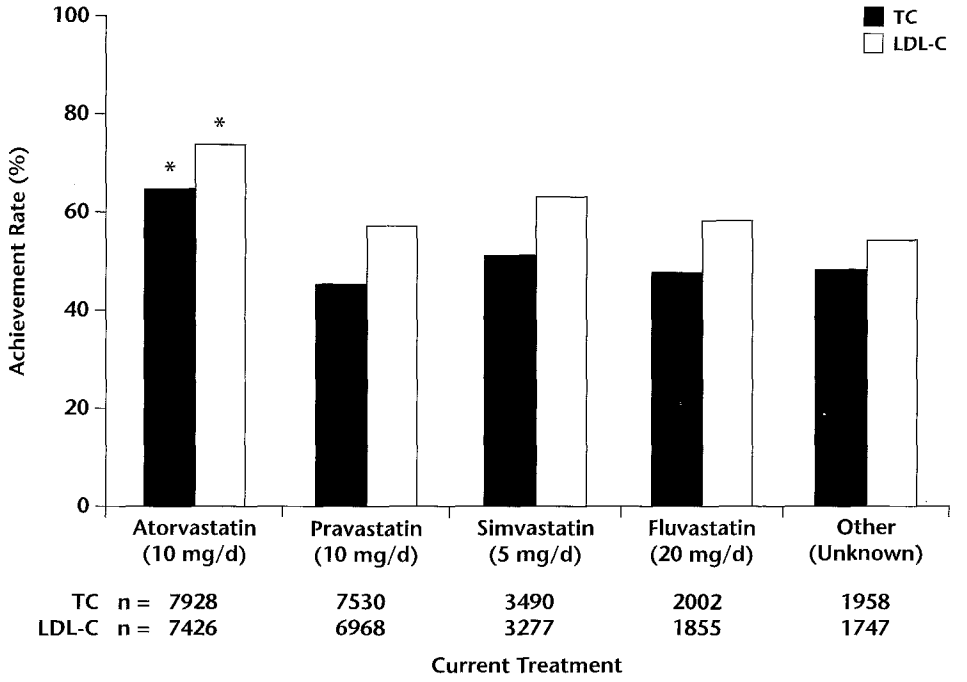

Figure 4. Rates of achievement of serum total cholesterol (TC) (n = 22,908) and low-density lipoprotein cholesterol (LDL-C) (n = 21,273) management goals after ≥3 months of lipid-lowering monotherapy at starting doses in patients with primary hyperlipidemia. *$P < 0.05$ versus all other treatments.

DISCUSSION

Clinical research in Japan and elsewhere has shown that the risk for CHD can be reduced by decreasing cholesterol levels.[1-6] Based on these findings, SLMGs are included in the treatment guidelines in Japan and elsewhere for the prevention of CHD. However, rates of achieving SLMGs have been shown to be unsatisfactory worldwide. For example, the Lipid Treatment Assessment Project,[13] a US survey, found that 38% of patients achieved the LDL-C goals recommended in NCEP ATP II.[14] Thirty-six percent of patients in the Belgian/Luxembourg Survey on Achievement of European Atherosclerosis Society Lipid Goals[15] achieved LDL-C goals in the Recommendation of the European Atherosclerosis Society.[16]

Administering statin-based lipid-lowering therapy to persons irrespective of their initial cholesterol concentrations or hypertensive patients at high risk for CHD significantly reduces the risk for CHD and myocardial infarction.[17,18] Statins exhibit pleiotropic effects (including anti-inflammatory and antioxidative effects)[19] that are thought to increase the usefulness of statin-based lipid-lowering therapies for the prevention of CHD.

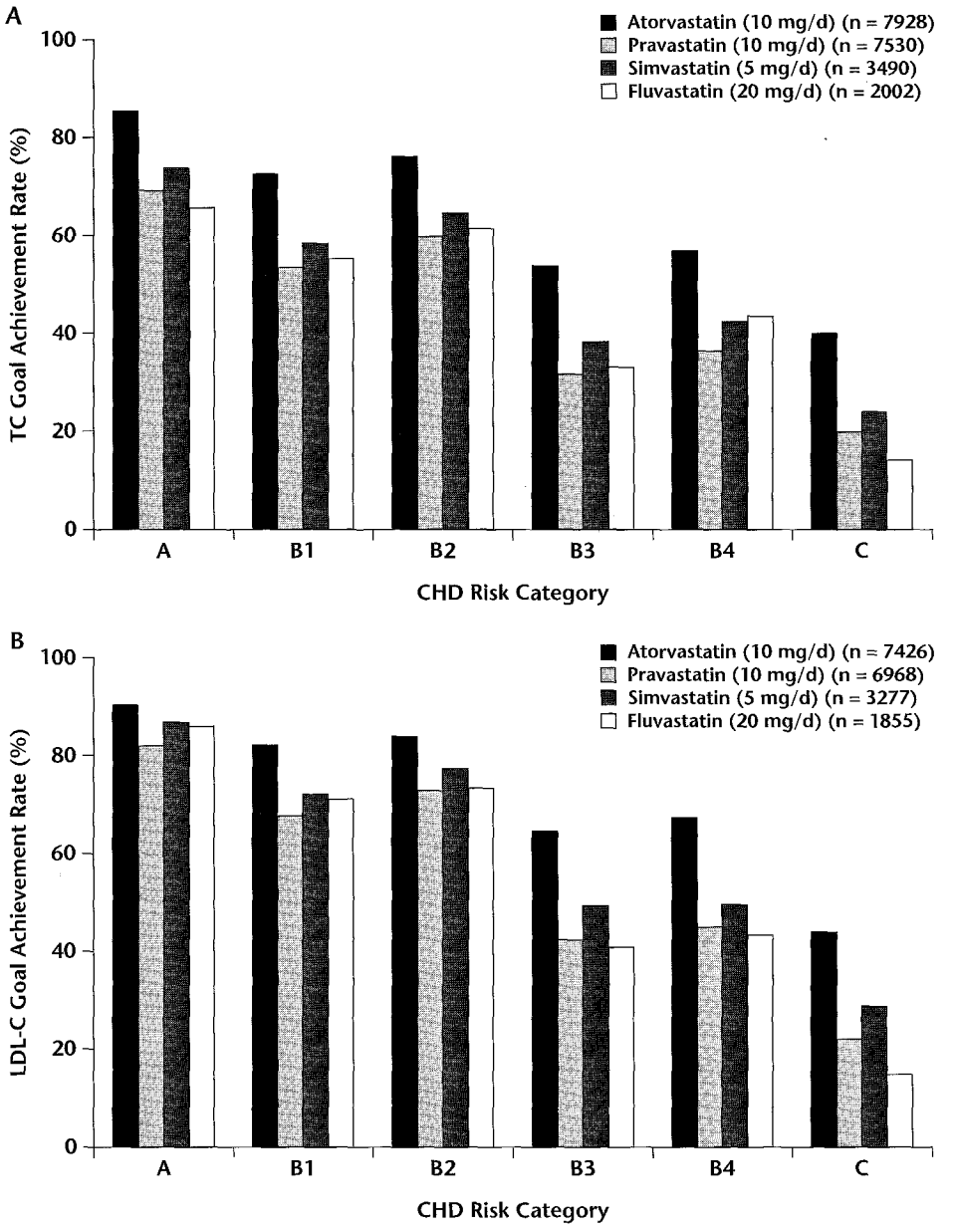

Figure 5. Rates of achievement of serum total cholesterol (TC) (n = 23,840) (A) and low-density lipoprotein cholesterol (LDL-C) (n = 22,121) (B) management goals by coronary heart disease (CHD) risk category after ≥3 months of lipid-lowering monotherapy with the starting doses of statins in patients with hyperlipidemia. See **Table I** for definitions of risk categories.

In the present study, the distribution of patients across Japan corresponded closely to the by-prefecture population distribution in Japan. Thus, the data collected are thought to allow a proper assessment of nationwide therapy status.

This survey included a large number of elderly patients (aged >65 years) and women (whose CHD risk is higher than that of men[8]). Clinical studies reported after the first guideline[7] was published have demonstrated the efficacy of lipid-lowering therapy in the elderly.[20,21] J-LIT[5] focused on both the elderly aged 65 to 70 years and aged ≤64 years with TC levels >270 mg/dL on enrollment. This trial showed that TC levels decreased to ≤270 mg/dL during follow-up and LDL-C levels decreased to ≤130 mg/dL (from ≥180 mg/dL at baseline), with lipid-lowering drugs. The absolute reduction in patients aged 65 to 70 years was similar to that in patients aged ≤64 years.[5] Thus, patients aged ≥65 years were included in the present study.

We found that 87.1% of patients prescribed lipid-lowering therapy were classified as category B, with most of those patients falling into categories B1 to B3. The JAS classifies patients with DM-2 and/or IGT, which is considered a coronary risk factor, as B3 risk equivalent. A total of 70.1% of the patients in category B3 had DM-2 and/or IGT in addition to other risk factors, whereas 2.7% of patients had DM-2 and/or IGT as the sole risk factor. The stratification of patients by detailed risk categories might help health care professionals produce optimal risk-reduction programs for the prevention of CHD.

The rates of achieving the TC and LDL-C goals (53.1% and 63.4%, respectively) are not satisfactory because successful attainment of NCEP goals[11] ranges from 40% to 50%.[14] In contrast, the rate of achieving the HDL-C goal (92.6%) was satisfactory based on NCEP attainment goals.[11] Although the LDL-C goals recommended in JAS 2002[8] are comparable to those in NCEP ATP III,[11] the JAS provides more detailed risk categories based on lipid levels (**Table I**). Briefly, NCEP ATP III[11] recommends LDL-C–lowering therapy for the primary prevention of CHD based on the Framingham CHD Risk Assessment Tool[22–24] and a CHD risk classification that uses just 2 categories: ≤1 coronary risk factor (low to moderate) and ≥2 coronary risk factors (high). Although both guidelines were developed for clinicians managing patients with elevated LDL-C levels, the JAS provides criteria for achieving LDL-C goals using more intensive drug therapy based on more CHD risk categories.[9]

In the present study, TC goals were achieved by ~60% to 80% of patients in categories A, B1, and B2; LDL-C goals were achieved by ~70% to 90% of patients in these categories. However, in patients in categories B3 to C, the rates were unsatisfactory: 27.4% of patients in category C achieved the TC goals. These findings suggest the need for more aggressive lipid-lowering therapy for patients at high coronary risk.

The mean serum TC and LDL-C levels were statistically similar in patients in all CHD risk categories (TC, ~210 mg/dL; LDL-C, 120 mg/dL). Few patients in category C were prescribed high doses of a statin even though many failed to achieve the SLMGs. This finding suggests that physicians in the present

study might have prescribed therapy based on JAS 1997,[7] in which the TC goal was <220 mg/dL. Although it is essential to prescribe lipid-lowering therapy based on the pathology in the individual patient, it is hoped that patients at high risk for CHD are treated according to the current JAS recommendations,[8,9] in which more intensive therapy is recommended to achieve the SLMGs.

The present study suggests that the statins as second-line therapy are effective in normalizing TC and LDL-C levels. Compared with the other statins, atorvastatin and simvastatin were associated with greater reductions in TG level (**Table II**) (both, $P < 0.05$ vs pravastatin and fluvastatin). Overall, patients prescribed atorvastatin had the highest SLMG achievement rates. Based on the fact that all of the drugs were prescribed at their starting doses, it might be concluded that the effectiveness of atorvastatin is not dose dependent but rather is attributable to its innate action. However, it should be noted that, because up-titration of the other drugs is ineffective, physicians might not be prescribing the appropriate doses. In the present study, treatment was up-titrated in 3.5% of patients. Based on this finding, if a physician prescribes drugs at their starting doses, treatment success is more likely to be expected.

Switching from a nonstatin to a statin or from one statin to another (14.7% or 84.0% of the total population, respectively) was associated with improved lipid levels and increased achievement rates, which prompted the JAS recommendation to switch patients not achieving their goals to another therapeutic drug.

Patients with FH (3.4% of the study population) were not prescribed a higher mean dose of any drug than patients with primary hyperlipidemia. Rates of achieving TC and LDL-C goals based on category C standards were both low—~10%—suggesting a need to treat patients with FH more aggressively.

CONCLUSIONS

The results of this study of Japanese patients undergoing lipid-lowering therapy for the prevention of CHD, prescribed based on the JAS recommendations, suggest insufficient reduction of TC, LDL-C, and TG in patients at high risk for CHD and the need for more aggressive lipid-lowering therapy in such patients.

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