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LDL-cholesterol goal attainment under persistent lipid-lowering therapy in northeast China

Subgroup analysis of the dyslipidemia international study of China (DYSIS-China)

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Abstract

Lipid-lowering therapy with statins reduces the risk of cardiovascular events, but the efficacy of persistent treatment in a real-world setting may vary from regions. Routine lipid-lowering therapy in the region with a high prevalence of cardiovascular disease may lead to more failures of goal attainment. We therefore performed a study to observe different lipid-lowering strategies in northeast (NE) China with respect to low-density lipoprotein-cholesterol (LDL-C) reduction and goal attainments.

A cross-sectional study (DYSIS-China) was conducted in 2012, involving 25,317 patients from 122 centers across China who were diagnosed with hyperlipidemia and treated with lipid-lowering therapy for at least 3 months. Of these patients, 4559 (18.0%) were assigned to the NE group according to their residential zones.

Patients in the NE group tended to be younger, female, overweight, and had more comorbidities and higher blood lipid levels than those in the non-NE group ($P < .001$). The goal attainment for LDL-C in NE was lower than non-NE (45.3% vs 65.1%, $P < .001$), and especially lower in high (NE vs non-NE, 38.5% vs 58.6%) and very high (NE vs non-NE, 22.6% vs 43.7%) risk patients. The proportion of high intensity statin was lower in NE than non-NE, and the proportion of combination therapy was similar (~2%). However, the goal attainment did not increase after administering higher dosages of statins in 2 groups. Logistic regression analysis identified diabetes mellitus (DM), coronary heart disease (CHD), cerebrovascular disease (CBD), being female, body mass index (BMI) >24 kg/m^2, drinking alcohol, smoking, and being residence in NE China as independent predictors of LDL-C attainment.

Despite having received persistent lipid-lowering treatments, the current situation of dyslipidemia patients in NE China is unsatisfactory. The main treatment gap might be related to the choice of statin and effective combination therapy and the control of comorbidities and obesity, especially for high-risk patients.

Abbreviations: NE = Northeast, LDL-C = low-density lipoprotein cholesterol, DM = diabetes mellitus, CHD = coronary heart disease, CBD = cerebrovascular disease, BMI = body mass index, CVD = cardiovascular disease, CTT = Cholesterol Treatment Trialists' Collaboration, SD = standard deviation, TC = total cholesterol, TG = triglycerides.

Keywords: DYSIS, dyslipidemia, epidemiology, LDL-C, statins

1. Introduction

Low-density lipoprotein-cholesterol (LDL-C) is an established and modifiable risk factor for cardiovascular disease (CVD) patients.[1,2] Reduction of LDL-C with a statin can decrease the risk of major vascular problems and one-fifth reduction of heart attack incidence, revascularization, and ischemic stroke can be achieved with a LDL-C reduction of 1.0 mmol/L each year[3] and the clinical benefit of using statins is proportional to the absolute reduction in LDL-C serum concentrations, which was noted by the Cholesterol Treatment Trialists' Collaboration (CTT).[4] Although current guidelines emphasize that the lowering of LDL-C with statin treatments is important for blood cholesterol control, questions still remain about the selection of statin treatment intensities in different populations. Compared with North American and European, East Asians were reported to have superior statin responsiveness and lower LDL-C baseline serum concentrations, and especially a Japanese study showed that only 10 to 20 mg/day of pravastatin could already lead to approximately 25% reduction of LDL-C levels.[5] Similarly, the results from the HPS2-THRIVE study also indicated that Chinese patients achieved lower LDL-C serum concentrations after identical lipid-lowering drug therapies than Europeans,[6] which

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is supported by the finding that plasma exposure to rosuvastatin was significantly higher in Asian than in Caucasian people.[7] In addition, LDL-C baseline serum concentrations in East Asian countries were reported to be lower than Caucasians ranging from 3.30 to 3.50 mmol/L.[8,9] In addition, there is a crucial safety concern for using statins in China, as an increased incidence of myopathy and elevated aminotransferase levels has been noted particularly in Asian patients for which high-intensity statin medication is recommended with certain limitations.[1,10]

The efficacy of persistent lipid-lowering therapy in real-world settings may vary among regions as different lifestyles and characteristics of diet. In the past 30 years, total cholesterol (TC) serum concentrations fell in high-income regions such as Australasia, Western Europe, and North America by about 0.2 mmol/L per decade, whereas mean TC serum levels increased in Southeast and East Asia as well as in the Pacific region by 0.08 to 0.09 mmol/L per decade.[11] Particularly in China, blood cholesterol levels are also increasing due to rapid economic growth and changes in lifestyle and diet,[12,13] and a previous study has reported a 23.9% (0.91 mmol/L) increase in TC and a 42.7% (0.47 mmol/L) increase in triglycerides (TGs) during a 5-year period.[14]

However, research about Chinese chronic disease monitoring showed that the prevalence of hypercholesterolemia in eastern China (4.2%) was significantly higher than in the middle (2.4%) and western (3.1%) regions.[15] In addition, the prevalence of dyslipidemia (62.1%) in NE China was essentially higher than the average for China as a whole,[16] while the overall prevalence of metabolic syndrome in the NE Jilin province has been reported to be as high as 32.86% as a result of a genetic predisposition combined with environmental factors.[17]

In the present study, we selected NE China, a region with a high incidence of CVD, and aimed to observe the goal attainment after persistent lipid-lowering therapy based on current guidelines and try to find out possible risk factors. The results of the present study could provide the evidence for choosing optimal lipid-lowering therapy for those living in regions with a high risk of developing CVD.

2. Methods

2.1. Patient population and study design

DYSIS is a cross-sectional epidemiological study, involving many institutions worldwide. DYSIS-China included 25,697 patients from 122 centers across China from April 2012 to October 2012.[6] The study was purely observational, as the diagnosis and treatment of patients was unaltered; however, all data were carefully recorded. Consecutive outpatients were selected in case they were $>$ 45 years old and currently treated with a lipid-lowering drug. Criteria for patient inclusion were an accurate fasting lipid profile assessed after 6 months lipid-lowering treatment and for at least 3 months, without any alteration in the drug dosage for 6 weeks or more. The solely exclusion criterion was that the patient has already participated in a previous clinical study. The study was approved by the ethical committees of the participating hospitals and all patients provided written informed consent before entering the study

After exclusion of 380 (1.48%) patients from which lipid parameters were inappropriate or missing, finally, a total of 25,317 patients were included for analyses. The patients who came from NE China were included in the NE group, which included 3 provinces (Fig. 1) and the other patients were combined in the non-NE group.

2.2. Data measurements and collection

The clinical examination and medical charts from single outpatient visits were collected. Information about smoking status, medication use, comorbidities including hypertension, diabetes mellitus (DM), and CVD were obtained via self-reporting of a face-to-face counseling method. It was important to document the medication records of patients receiving constant treatments that included various lipid-lowering agents drugs such as nicotinic acid, fibrates, cholesterol absorption inhibitors as well as statins, and the traditional Chinese medicine Xuezhikang. The identity and the daily dose of the lipid-lowering agents taken by each patient during the previous 6 months and at the time of a visit were documented. Furthermore, antihypertensive, antidiabetic as well as antiplatelet drug usage was recorded. The research team trained a series of investigators for the research project that included cardiologists, endocrinologists, geriatricians, internists, and neurology specialists.

2.3. Treatment goals and risk classification

In this study, we used NCEP-ATP III criteria and the 2007 Chinese guidelines as dyslipidemia management criteria for the risk classification of CVD patients and definition of LDL-C goal attainment rates. On the basis of NCEP-ATP III criteria, the LDL-C target values were defined for low risk [$<$4.1 mmol/L (160 mg/dL)], moderate risk [$<$3.4 mmol/L (130 mg/dL)], moderate-high risk [$<$ 3.4 mmol/L (130 mg/dL)], high risk [$<$2.6 mmol/L (100 mg/dL)], and very high-risk patients $<$ 1.8 mmol/L (70 mg/dL). According to the 2007 Chinese Guidelines criteria, the LDL-C target values for dyslipidemia patients were categorized into low-risk (10-year risk score of ischemic CVD $<$ 5%), [$<$ 4.1 mmol/L (160 mg/dL)], moderate-risk (10-year risk score 5–10%), [$<$3.4 mmol/L (130 mg/dL)], high-risk (CHD or other atherosclerotic vascular disease, DM, or 10-year risk score 10–15%), [$<$ 2.6 mmol/L (100 mg/dL)], and very high-risk [with acute coronary syndrome (ACS) or CHD and DM], [$<$2.0 mmol/L (80 mg/dL)] groups.

2.4. Statistical analysis

Continuous quantitative variables are reported as the mean $\pm$ standard deviation (SD) and descriptive data are used as frequencies expressed as percentages. Comparison among categorical and continuous variables are calculated with Pearson χ^2 and Student t test, respectively. A multiple linear regression model was used to evaluate the variation trend of the control rate, which was adjusted for age, sex, and medication. To evaluate the independent risk factors for LDL-C level abnormalities in NE and non-NE patients, we performed a multiple logistic regression analysis. All data were analyzed with SAS, version 9.3 (SAS Institute Inc., Cary, NC). A P-value $<$ .05 was considered to be statistically significant.

3. Results

3.1. Patients and blood lipid levels

Overall, 25,317 consecutive outpatients from 122 centers were enrolled in the present study. Of these, 4559 (18.0%) patients

Figure 1. Map of the Chinese northeast (NE) region from which patients were recruited as a NE-derived cohort (Heilonjiang, Jilin, and Liaoning provinces).

were assigned to the NE group and 20,758 (82.0%) to the non-NE group. Table 1 revealed that patients in the NE group tended to be younger, female, overweight, and with higher average blood pressures and more comorbidities such as DM, CVD, and heart failure (HF). The levels of individual components of the lipid profiles showed significant differences between 2 groups. TC, LDL-C, TGs, and nonhigh-density lipid cholesterol (non-HDL-C) were all significantly higher in NE than non-NE. Also, we found a higher proportion of patients in the 10-year CVD high or very high-risk levels, as well as that of drinking and smoking in the NE group.

3.2. Lipid-lowering therapies

Almost all patients (~98%) were receiving monotherapy (NE vs non-NE, 98.1% vs 97.7%, $P=.457$); thus, the percentage of combination therapy was very small. The most prescribed agent for monotherapy was a statin in both groups (NE 86.0% vs non-NE 89.5%, $P<.001$). Atorvastatin (NE 28.1% vs 38.3%, $P<.001$) 191.75 and simvastatin (NE 42.6% vs non-NE 34.4%, $P<.001$) were the most frequently prescribed statins, followed by rosuvastatin (NE 8.2% vs non-NE 8.3%, $P=.685$), fluvastatin (NE 2.4% vs non-NE 2.5%, $P=.973$), lovastatin (NE 0.2% vs non-NE 0.8%, $P<.001$), pitavastatin (NE 2.1% vs non-NE 0.2%, $P<.001$), and pravastatin (NE 0.5% vs non-NE 3.8%, $P<.001$) (Table 2).

The usual doses for statins as monotherapies were potency 3 and potency 4 (Fig. 2), which equated to a dosage of simvastatin of 20 to 40 mg or moderate-intensity statins. The proportion of patients treated with potency 1 and potency 2 were higher in NE than in non-NE patients, while the proportion of patients treated with potency 4 and 5 were lower in NE than in non-NE patients. Only 2.0% of patients received combination therapy with no statistical difference between the 2 groups ($P=.0561$) (Table 2).

3.3. LDL-C goal attainments

Overall, the LDL-C goal attainment rate in the NE group was significantly lower than that in the non-NE group based on NCEP-ATP III criteria (45.3% vs 63.3%) and 2007 Chinese

Table 1

Patient characteristics.

Variables	NE (N = 4559)	Non-NE (N = 20,758)	*P*
Age, (Mean ± SD, y)	63.48 ± 10.101	65.79 ± 10.528	<.0001
≥65 y, (N, %)	1998, 43.83	11,102, 53.48	<.0001
Sex, male, (N, %)	2168, 47.55	10,807, 52.06	<.0001
BMI, (Mean ± SD, kg/m^2)*	25.09 ± 3.230	24.62 ± 3.273	<.0001
≥24 kg/m^2, (N, %)	2923, 64.11	11,833, 57.00	<.0001
Hemoglobin A1c, (Mean ± SD, %)†	7.82 ± 2.079	7.12 ± 1.809	<.0001
SBP, (Mean ± SD, mm Hg)‡	135.4 ± 16.67	129.9 ± 15.21	<.0001
DBP, (Mean ± SD, mm Hg)‡	81.7 ± 9.94	77.4 ± 9.50	<.0001
Smoking history	711, 15.6	2432, 11.7	<.0001
Drink history	589, 12.9	1714, 8.3	<.0001
Sedentary lifestyle	761, 16.7	4236, 20.4	<.0001
Comorbidities			
Hypertension, (N, %)	2588, 56.8	14,062, 67.7	<.0001
Diabetes, (N, %)	1641, 36.0	7134, 34.4	.0381
CHD, (N, %)	17,18, 37.7	7702, 37.1	.4736
Cerebrovascular disease, (N, %)	983, 21.6	3298, 15.9	<.0001
Heart failure, (N, %)	217, 4.8	752, 3.6	.0003
Perivascular disease, (N, %)	36, 0.8	227, 1.1	.0798
10-y CVD risk level§			
Very high, (n/N, %)	588, 12.9	2504, 12.06	<.0001
High, (n/N, %)	2815, 61.7	12,101, 58.30	<.0001
Moderate, (n/N, %)	435, 9.5	2347, 11.31	<.0001
Low, (n/N, %)	721, 15.8	3806, 18.34	<.0001
Lipid profile, mmol/L			
TC (Mean ± SD)	4.82 ± 1.188	4.54 ± 1.204	<.0001
LDL-C (Mean ± SD)	3.00 ± 1.003	2.54 ± 0.945	<.0001
TG (Mean ± SD)	1.98 ± 1.548	1.87 ± 1.423	<.0001
HDL-C (Mean ± SD)	1.26 ± 0.370	1.28 ± 0.381	.0013
Non-HDL-C (Mean ± SD)	3.56 ± 1.128	3.26 ± 1.143	<.0001

NE referred to NE group.

BMI = body mass index, CBD = cerebrovascular Disease, CHD = coronary heart disease, DBP = diastolic blood pressure, DM = diabetes mellitus, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure, TC = total cholesterol, TG = total glyceride.

* Data on 25,308 patients were available (4559 for NE, 20,749 for non-NE).

† Data on 5950 patients were available (1165 for NE, 4,785 for non-NE).

‡ Data about 25,311 patients were available (4558 for NE; 20,753 for non-NE).

§ According to the Chinese 2007 criteria.

Guidelines criteria (45.3% vs 65.1%; $P < .001$), as well as in the almost all risk groups. In the different statins monotherapy groups, non-NE group had higher goal attainment rate in potency 2, 3, 4, and 5 than NE group, although there was no difference in patients with combination therapies (Table 3). The achievement rates in different cardiovascular risk subgroups showed a downward trend with the increased risk of cardiovascular events in both groups (Table 4).

Table 2

The lipid-lowering therapies.

Treatment pattern	Generic name	NE (N = 4559, %)	Non-NE (N = 20,758, %)	*P* (NE vs non-NE)	*P*
Monotherapy		4473, 98.1	20,328, 97.9	.4574	.4574
	Statins	3847, 86.0	18,192, 89.5	<.0001	<.0001
	Atorvastatin	1295, 28.1	7785, 38.3	<.0001	<.0001
	Lovastatin	8, 0.2	168, 0.8	<.0001	
	Pravastatin	21, 0.5	789, 3.8	<.0001	
	Simvastatin	1940, 42.6	7146, 34.4	<.0001	
	Fluvastatin	110, 2.4	522, 2.5	.9730	
	Rosuvastatin	375, 8.2	1732, 8.3	.6853	
	Pitavastatin	98, 2.1	50, 0.2	<.0001	
	Xuezhikang	227, 5.0	1019, 4.9	.8931	
	Fibrates	285, 6.3	972, 4.7	<.0001	
	Nicotinic Acid	5, 0.1	15, 0.1	.6034	
	Ezetimibe	1, 0.0	22, 0.1	.1540	
	Others	108, 2.4	108, 0.5	<.0001	
Combination therapy		86, 1.9	430, 2.1	.4574	.0561
	Dual	84, 1.8	418, 2.0	.8085	
	Triple	1, 0.0	12, 0.1	.6035	
	Quadruple	1, 0.0	0, 0.0	.3706	

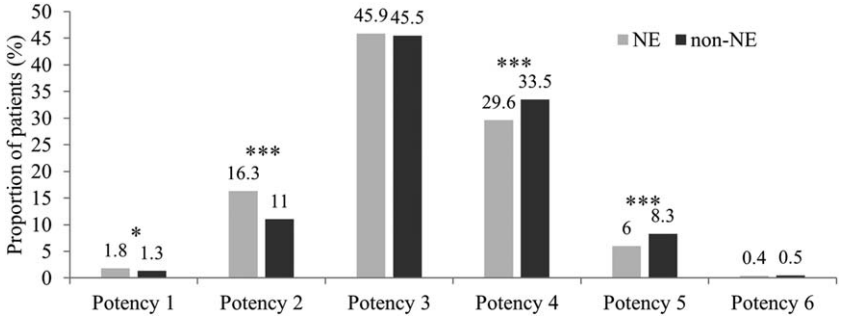

Figure 2. The comparison of different statin potencies treatment. Potency 1: is equivalent to simvastatin 5 mg/day; Potency 2 is equivalent to simvastatin 10 mg/day; Potency 3 is equivalent to simvastatin 20 mg/day; Potency 4 is equivalent to simvastatin 40 mg/day; Potency 5 is equivalent to simvastatin 80 mg/day; Potency 6 is equivalent to simvastatin 160 mg/day. $^{*}P<.05$, $^{**}P<.01$, $^{***}P<.001$.

Table 3

The goal attainment rates in different statin potencies and therapies.

Medications	Total patients	Goal attainment of 3,837 NE patients (N, %)	Goal attainment of 18,026 non-NE patients (N, %)	*P*
Statins as monotherapy	24,801	2027/3837 (52.8)	13,232/18,026 (73.4)	<.0001
Potency 1	299	44/68 (64.7)	148/231 (64.1)	1.0000
Potency 2	2605	273/627 (43.5)	1239/1978 (62.6)	<.0001
Potency 3	9958	730/1763 (41.4)	5284/8195 (64.5)	<.0001
Potency 4	7179	554/1134 (48.9)	3993/6045 (66.1)	<.0001
Potency 5	1725	106/231 (45.9)	977/1494 (65.4)	<.0001
Potency 6	96	5/14 (35.7)	52/82 (63.4)	.0761
Statin combination therapy*	502	38/84 (45.2)	263/418 (62.9)	.0033
Atorvastain + Others	116	6/15 (40.0)	71/101 (70.3)	.0369
Simvastain + Fibrates	61	1/5 (20.0)	35/56 (62.5)	.1488
Atorvastatin + Fibrates	47	3/4 (75.0)	26/43 (60.5)	1.0000
Simvastain + Others	47	10/16 (62.5)	19/31 (61.3)	1.0000
Simvastain + Xuezhikang	30	3/10 (30.0)	9/20 (45.0)	.6942

* This contains only dual therapy rather than triple (13 patients) or more combination therapies (1 patient) because few patients used them.

3.4. Risk factors

Next, we analyzed the independent risk factors for failure to achieve LDL-C target goals in both NE and non-NE dyslipidemia patients. Factors such as age, gender, smoking, drinking, BMI, DM, CHD, CBD, HF, combination therapy, and NE were entered into the stepwise logistic regression model. Table 5 summarizes that the independent risk factors ($P<.05$) for failure to achieve LDL-C target were comorbidities such as DM, CHD, and CBD and demographic variables such as being female, BMI $>24\,kg/m^2$, drinking alcohol, and a NE origin according to the NCEP-ATP III and 2007 Chinese Guideline criteria. In addition, we analyzed the risk factors for not achieving LDL-C goal attainments in NE or in non-NE patients separately (Supplementary Table 1, http://links.lww.com/MD/B967) and found that factors such as DM, CBD, CHD, and obesity (BMI $>24\,kg/m^2$) were related to the failure of goal attainment in the NE patients.

We further assessed the LDL-C goal attainment rate of the subgroup patients with CHD, DM, or CBD between the 2 groups

Table 4

The goal attainment rates in different risk groups.

Risk classification	NE (N = 4559)	Non-NE (N = 20,758)	*P*
NCEP-ATP III Criteria, (n/N, %)	2065/4559, 45.3	13,131/20,758, 63.3	<.0001
Very high, (n/N, %)	172/1095, 15.7	1259/4308, 29.3	<.0001
High, (n/N, %)	829/2188, 37.9	5754/9748, 59.0	<.0001
Moderate high, (n/N, %)	29/44, 65.9	236/280, 84.3	<.0001
Moderate, (n/N, %)	33/39, 84.6	224/268, 83.6	.8703
Low, (n/N, %)	1004/1193, 84.2	5658/6154, 91.9	<.0001
Chinese 2007 Criteria, (n/N, %)	2066/4559, 45.3	13,505/20,758, 65.1	<.0001
Very high, (n/N, %)	133/588, 22.6	1093/2504, 43.7	<.0001
High, (n/N, %)	1084/2815, 38.5	7090/12,101, 58.6	<.0001
Moderate, (n/N, %)	226/435, 52.0	1815/2347, 77.3	<.0001
Low, (n/N, %)	623/721, 86.4	3507/3806, 92.1	<.0001

NE referred to NE group, Non-NE referred to Non-NE group.
LDL-C = low-density lipoprotein cholesterol.

Table 5

Multivariate analysis.

	NCEP-ATP III criteria		2007 Chinese guidelines criteria	
	OR (95%CI)	P	OR (95% CI)	P
NE vs non-NE	2.15 (2.00–2.31)	<.001	2.26 (2.11–2.42)	<.001
Gender (female vs male)	1.67 (1.57–1.77)	<.001	1.57 (1.48–1.67)	<.001
DM (yes vs no)	4.17 (3.93–4.42)	<.001	3.03 (2.87–3.21)	<.001
CHD (yes vs no)	4.16 (3.91–4.43)	<.001	1.67 (1.57–1.77)	<.001
CBD (yes vs no)	2.01 (1.87–2.17)	<.001	1.49 (1.38–1.60)	<.001
HF (yes vs no)	0.77 (0.67–0.90)	.001	0.71 (0.62–0.82)	<.001
Age (≥65 vs < 65 y)	0.89 (0.84–0.94)	<.001	1.19 (1.12–1.24)	<.001
BMI (>24 vs ≤24 kg/m^2)	1.18 (1.11–1.25)	.031	1.18 (1.12–1.25)	<.001
Drinking (yes vs no)	1.11 (1.00–1.24)	.043	1.20 (1.09–1.33)	<.001
Smoking (yes vs no)	1.15 (1.04–1.26)	.005	1.18 (1.08–1.29)	<.001
Combination therapy (combination vs mono)	2.17 (2.02–2.33)	<.001	2.28 (2.13–2.45)	<.001

This table summarized the multivariate logistic regression analysis of factors associated with failure to achieve low-density lipoprotein cholesterol goal. NE referred to NE group. Combination therapy refers to using 2 or more types of lipid-lowering drugs, except for statins. Monotherapy refers to using statins as lipid-lowering therapy.
BMI = body mass index, CBD = cerebrovascular disease, CHD = coronary heart disease, DM = diabetes mellitus, HF = heart failure.

(Table 6). The NE group showed a lower control rate in all subgroups (all $P < .001$), regardless of being based on 2007 Chinese Guidelines criteria (CHD, 37.7% vs 59.7%; DM, 31.1% vs 48.3%; CBD, 32.9% vs 54.1%) or NCEP-ATP III criteria (CHD, 26.6% vs 47.2%; DM, 28.5% vs 43.8%; CBD, 36.5% vs 59.0%), which suggested that DM, CHD, and CBD are stronger risk factors for failure to achieve LDL-C goal attainments in NE than non-NE dyslipidemia patients.

4. Discussion

With the development of the economy and changes in lifestyles, dyslipidemia in China has gone into an adverse trend of increasing development.[11,18] A meta-analysis indicated that the prevalence of dyslipidemia had more than doubled in the last 10 years.[19] Our research found that NE patients, who had already accepted the treatment of lipid-lowering drugs for 3 months, had a higher cholesterol level than in other regions of China, indicating that there was a regional difference in the effect of lipid-lowering therapy. Regional variations of dyslipidemia have also been described for Canada[20] and racial as well as cultural differences have been attributed to the disparities. Similar to the US, in China, a stroke belt has also been proposed[21] in which the northern part of China as well as Tibet are regions with high incidences. The reasons for the higher stroke rates have been proposed to be a cold climate related dietary differences leading to higher BMIs and hypertension rates,[22] while the living environment of NE China is similar to Siberia and eastern Mongolia.

The results of the present showed that the control rate of LDL-C in the NE group was significantly lower than in the non-NE groups, especially in patients associated with a high risk of cardiovascular events. Current guidelines recommend statins as the choice of therapy for reducing LDL-C levels and preventing adverse cardiovascular events[1] and our results showed that statin-based monotherapy was the main lipid-lowering therapy in NE-China, but the usage of statin intensity was different. Although the proportion of moderate to high intensity in NE was a little lower than non-NE, the achievement rates of LDL-C did not increase with the increasing statin dosage in both groups. The CHILLAS study showed that only half of the patients reached the goal attainment for LDL-C (80 mg/dL) using double-dose atorvastatin (20–40 mg) in patients with ACS.[23] Even after administering atorvastatin at the highest dose (80 mg), many patients still failed to achieve their goal[24,25] and a meta-analysis of 38,153 patients showed that 40% patients given a high dose of atorvastatin or rosuvastatin did not reach the goal for controlling LDL-C.[26] The intensive statin therapy did not lead to a significant increase in achievement rates, even decreased in the NE region, which raised a question of whether the strong recommendation of intensive statin therapy in China (or East Asia) was really necessary, whether the moderate intensity statin was enough, and whether there were more effective combination therapies.

The multivariate logistic regression analysis carried out in this study indicated that combination therapy could not improve the LDL-C control rate in patients compared with monotherapy. However, only about 2% of patients in the present study were

Table 6

Subgroup analysis.

	CHD		DM		CBD	
	Goal attainment rate	P	Goal attainment rate	P	Goal attainment rate	P
2007 Chinese Guidelines criteria		<.0001		<.0001		<.0001
NE	37.7% (n = 648)		31.1% (n = 511)		36.5% (n = 359)	
Non-NE	59.7% (n = 4598)		48.3% (n = 3449)		59.0% (n = 1945)	
NCEP-ATP III criteria		<.0001		<.0001		<.0001
NE	26.6% (n = 457)		28.5% (n = 468)		32.9% (n = 323)	
Non-NE	47.2% (n = 3639)		43.8% (n = 3127)		54.1% (n = 1785)	

CBD = cerebrovascular disease, CHD = coronary heart disease, DM = diabetes mellitus.

treated with statin combination therapies, and 38.9% of them were treated with omega-3 fatty acids, 25.4% with fibrates, 9.0% with HypoCol, whereas only 7% of them were treated with ezetimibe combined with a statin, which is in disagreement with current ACC guidelines. The guidelines recommend adding ezetimibe to ongoing statin therapy, when LDL-C goals are not achieved by sole administration of a statin,[27] as the IMPROVE-IT trial and other studies revealed that when ezetimibe was combined with statin therapy, an additional lowering of LDL-C level was achieved.[28–30]

The low LDL-C goal attainment was also related to increased comorbidities, being aged <65 years, being female, and overweight (BMI >24 kg/m^2), which were consistent with previous studies.[31] Among individuals with a BMI >24 kg/m^2, it was unlikely to control dyslipidemia and the China REALITY survey showed a negative relationship between BMI and the attainment of the LDL-C goal.[32]

Taken together, the patients from NE China had higher HbA1c serum concentrations, though the diabetes incidence was not significantly different, indicating a higher percentage of metabolic syndrome cases, which was further supported by higher BMI, TC, LDL-C, TG, and non-HDL-C values, as has been previously reported for NE China.[33] In addition, the incidence of high and very high cardiovascular risk was significantly higher in NE than non-NE. Although these unfavorable conditions have seen enhanced monitoring in NE compared with non-NE dyslipidemia patients, the statin treatment intensity was significantly lower in them and LDL-C attainment rates were also significant lower, particularly in high and very high cardiovascular risk patients. Statin combination therapies were administered at extremely low rates in 2 groups and ezetimibe as a recommended statin combination drug was rarely used. We propose that the different lifestyle in the NE region of China with higher calorie intake and resulting BMI and blood lipid increases[21,22] might be a cause for higher cardiovascular risk factor incidence and particularly a less successful statin treatment rate, which otherwise in non-NE dyslipidemia patients is not that obvious. Especially for high-risk dyslipidemia patients with enhanced BMI, statin combination therapies with ezetimibe should be advocated in the NE of China, as with the lifestyles of these patients lend them more prone to develop more severe and less statin treatment-sensitive hyperlipidemias.

We have identified a number of limitations of the present study. First, the study was cross-sectional and observational and any long-term outcomes were not considered. It will be necessary to carry out a prospective follow-up study to determine the appropriate doses for individual patients treated with lipid-lowering agents and the goal attainment in relation to their relative mortality. Furthermore, lipid parameters were not measured in a central core laboratory. Finally, as lipid-lowering agent usage was an eligibility criterion for the patients, the goal attainment of all lipid parameters may have been overestimated, particularly for high-risk patients. In addition, other issues related to cholesterol metabolism such as genetic factors have not been included, as this study was only descriptive and results were limited to the available data from the DYSIS databank.

Despite having received persistent lipid-lowering treatments, the current situation of dyslipidemia patients in NE China is unsatisfactory. The main treatment gap might be related to the choice of lipid-lowering therapy including effective combination therapy especially for high-risk patients. Other concerns should include controlling weight and treating complications.

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