Cholesterol target value achievement and lipid-lowering therapy in patients with stable or acute coronary heart disease in Vietnam - results from the Dyslipidemia International Study II

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ABSTRACT

BACKGROUND

Patients with established coronary heart disease (CHD) and those who suffer an acute coronary syndrome (ACS) are at risk of recurrent adverse events. Hyperlipidemia is a major risk factor for cardiovascular disease; however, there is insufficient information available regarding the extent of lipid abnormalities and how they are managed in individual countries.

METHODS

The Dyslipidemia International Study (DYSIS) II was a multinational observational study involving subjects with stable CHD and those being hospitalized with an ACS. The present article concerns the subjects enrolled in Vietnam. A full lipid profile and utilization of lipid-lowering therapy (LLT) were documented at baseline, and for the ACS cohort, at 4 months after hospital discharge. Low-density lipoprotein cholesterol (LDL-C) target attainment as per European guidelines was assessed, and multivariate regression was performed in order to identify predictors for achieving an LDL-C level of <70 mg/dL.

RESULTS

A total of 612 patients were recruited from 4 sites in Vietnam, 407 with stable CHD and 205 with an ACS. At baseline, 95.8% of the CHD cohort and 73.7% of the ACS cohort were being treated with LLT. LDL-C levels were lower for treated than non-treated patients in both the CHD (89.2 vs. 120.8 mg/dL; $p < 0.01$) and ACS (90.2 vs. 112.6 mg/dL; $p < 0.01$) cohorts; accordingly, LDL-C target attainment was greater (CHD: 29.6% vs. 11.8%, $p = 0.11$; ACS: 33.8% vs. 14.8%, $p < 0.01$). By the 4-month follow-up, target attainment had increased significantly for the ACS patients (from 0.0% at baseline to 33.3% at 4-month), that had not originally been treated with LLT, which was in response to therapy initiation after hospitalization. However, there was little improvement for the patients that were already being treated prior to the ACS. Lipid levels were rarely re-checked in the 4 months after discharge from hospital.

CONCLUSIONS

The extent of hyperlipidemia is of significant concern for patients with CHD in Vietnam, with few patients displaying an LDL-C level at the recommended target. LLT was widely used, but was rarely maximized, indicating a need for improved monitoring and treatment of these very high-risk patients.

KEYWORDS

cholesterol, hyperlipidemia, statins, ezetimibe, acute coronary syndrome, myocardial infarction, lipids

INTRODUCTION

Cardiovascular disease is the most common cause of death in Vietnam. In 2008, the age-standardized mortality rate due to ischemic heart disease was 112.5 deaths per 100,000 people, which is similar to that for all types of cancer combined (113.7 deaths per 100,000).[1] Owing to the increasing prevalence of risk factors such as obesity, smoking, hypertension and hyperlipidemia, the burden of cardiovascular disease is set to continually rise.[2, 3] Effective management of these risk factors could significantly reduce mortality in Vietnam. In terms of hyperlipidemia, the Asia–Pacific Cohort Studies Collaboration (APCSC) reported that for every 39 mg/dL (1 mmol/L) increase in TC, the risk of death due to coronary heart disease (CHD) was approximately 35% higher.[4] Furthermore, Nguyen et al. estimated that 32% of deaths due to ischemic heart disease in the East Asia and Pacific region, including Vietnam, could be avoided by reducing total cholesterol (TC) to an optimal level of ≤150 mg/dL (3.8 mmol/L).[2]

Reducing levels of low-density lipoprotein cholesterol (LDL-C) specifically has been shown to greatly lower the risk of major adverse cardiovascular events.[5] Therefore, guidelines regarding the management of hyperlipidemia generally focus on reducing levels of this lipid. The European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

guidelines recommend a target LDL-C value of <70 mg/dL for patients considered to be at very high cardiovascular risk.[6] However, attainment of this target has been reported to be poor. In the Dyslipidemia International Study (DYSIS), only 21.7% of the very high-risk statin-treated subjects in the global cohort had an LDL-C level below 70 mg/dL.[7] This value is similar to the 22.8% reported for the very high-risk treated patients included in the global cohort of the Centralized Pan-regional Survey on the Undertreatment of Hypercholesterolemia (CEPHEUS).[8] The Pan-Asian cohort of CEPHEUS, however, had much better target attainment, at 34.9%.[9] Despite the superior goal achievement found in Asia, there appears to be a large proportion of patients at very high-risk for recurrent cardiovascular adverse events who have elevated LDL-C.

DYSIS II was established in order to quantify the global extent of hyperlipidemia in patients with stable and acute CHD. Using standardized methodology, lipid levels were evaluated at a country and global level. Furthermore, the approaches used in each country for lowering LDL-C were analyzed. The present article reports on the data gathered from patients in Vietnam.

METHODS

Study design and patients

DYSIS II was an observational, cross-sectional, multinational study. Subjects in Vietnam were enrolled from 4 sites from May to September 2014. Patients aged 18 years or over were included if they were either attending a clinic appointment for stable CHD or were being hospitalized with an ACS. Patients were excluded if they were participating in a clinical trial at the same time as the study, and for the ACS cohort, if they died whilst in hospital. Stable CHD was defined as documentation of stenosis greater than 50% as determined by either coronary angiography or cardiac CT, prior percutaneous coronary intervention (PCI), or prior coronary artery bypass grafting (CABG). ACS was defined as an ST-segment elevation myocardial infarction or left bundle branch block myocardial infarction (STEMI/LBBB-MI), a non-ST-segment elevation myocardial infarction (NSTEMI), or unstable angina (UA). Patients were required to have a full lipid profile available in order to be included in the study. For the CHD cohort this was taken from the last test within the 12 months prior to the outpatient appointment. For the ACS cohort, a new lipid profile was constructed from blood taken within 24 h of hospital admission. Patients were divided according to whether or not they were being treated with lipid-lowering therapy (LLT) at the time of the lipid test. In order to be included in the LLT groups, treatment duration had to be ≥3 months by the time of the test. Data regarding the CHD patients were collected at the clinic appointment and from medical records, while those for the ACS patients were collected at hospital admission and during a telephone interview 4 months later.

The study received approval from the ethics committee at each study center and was conducted in accordance with the Declaration of Helsinki and its amendments.

Documentation

The collected data were entered into an online database maintained at the Institut für Herzinfarktforschung (Ludwigshafen, Germany). For all patients, demographic and clinical variables were documented at baseline (outpatient appointment [CHD] or hospital admission [ACS]). These factors included age, gender, and body mass index (BMI); the presence of diabetes mellitus, hypertension, chronic kidney disease (CKD) or congestive heart failure (CHF); documentation of prior stroke (ischemic or hemorrhagic) or myocardial infarction (MI); and the presence of other cardiovascular risk factors, including smoking, a sedentary lifestyle and a family history of CHD. Diabetes was defined as current treatment for diabetes, a previous diagnosis of diabetes, or a fasting plasma glucose level of ≥126 mg/dL. Hypertension was defined as current blood-pressure-lowering treatment, a previous diagnosis of hypertension, or a blood pressure reading of >140/90 mm Hg. A sedentary lifestyle was defined as <20–30 minutes of walking on <3–4 days per week. Obesity was defined as a BMI of >30 kg/m^2.

The lipid profiles that were constructed for each patient included serum levels of LDL-C, high-density lipoprotein cholesterol (HDL-C), non-HDL-C, TC, and triglycerides. Each ACS patient was assigned to a pre-admission cardiovascular risk category according to the presence of comorbidities and additional risk factors, as defined in the 2011 ESC/EAS guidelines.[10] Each risk level was associated with a target LDL-C value (<70 mg/dL, <100 mg/dL, <115 mg/dL, and <130 mg/dL for the very high-risk, high-risk, moderate risk, and low-risk patients, respectively), and the proportions of patients that had attained their target were calculated. At the 4-month follow-up, when all ACS patients were considered to be at very high-risk due to the ACS event, LDL-C target attainment was evaluated for any subjects with a repeat lipid profile available.

The different forms of LLT that patients were being treated with were recorded at baseline, and for the ACS cohort, at the 4-month follow-up interview. Statin therapy that was documented included use of atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin, either as monotherapy or in combination with a non-statin. The non-statins

Table 1: Patient characteristics – stable CHD cohort

	All patients mean ± SD or % (n/N) (N = 407)	LLT mean ± SD or % (n/N) (N = 390)	No LLT mean ± SD or % (n/N) (N = 17)
Age (years)	65.0 ± 10.1	64.9 ± 10.0	66.2 ± 12.2
Male	69.8 (284/407)	69.7 (272/390)	70.6 (12/17)
BMI (kg/m^2)	23.7 ± 3.0	23.7 ± 3.0	22.4 ± 2.9
BMI > 30 kg/m^2	2.5 (10/407)	2.6 (10/390)	0.0 (0/17)
Comorbidities and CV risk factors			
Type 2 diabetes mellitus	34.6 (141/407)	34.9 (136/390)	29.4 (5/17)
Hypertension	71.0 (289/407)	71.3 (278/390)	64.7 (11/17)
CKD	13.5 (55/407)	13.8 (54/390)	5.9 (1/17)
History of stroke*	5.0 (20/403)	4.9 (19/387)	6.3 (1/16)
PAD	5.0 (20/402)	5.2 (20/386)	0.0 (0/16)
Current smoker	8.1 (33/407)	7.7 (30/390)	17.6 (3/17)
Sedentary lifestyle	18.3 (73/398)	18.6 (72/387)	9.1 (1/11)
Family history of CHD	6.6 (25/380)	6.6 (24/365)	6.7 (1/15)
CHD diagnosis			
Coronary angiography (stenosis >50%)	20.9 (85/407)	19.0 (74/390)	64.7 (11/17)
Cardiac CT (stenosis >50%)	4.2 (17/407)	3.8 (15/390)	11.8 (2/17)
Prior PCI	70.3 (286/407)	72.6 (283/390)	17.6 (3/17)
Prior CABG	14.5 (59/407)	15.1 (59/390)	0.0 (0/17)
History of ACS†	15.5 (63/407)	15.1 (59/390)	23.5 (4/17)

Legend: *Includes ischemic and hemorrhagic stroke; †>3 months prior to enrollment. LLT, lipid-lowering therapy; BMI, body mass index; CV, cardiovascular; CHD, coronary heart disease; CKD, chronic kidney disease; PAD, peripheral artery disease; CT, computed tomography; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; ACS, acute coronary syndrome. P-values calculated using chi-squared test or Mann–Whitney–Wilcoxon test.

included ezetimibe, nicotinic acid, fibrates, and omega-3 fatty acids. Statin dosages were normalized to atorvastatin potency according to clinical trial data regarding the lipid-lowering abilities of the different statins.[11]

For the ACS patients, the occurrence of adverse events during the 4-month follow-up period was documented. This included death, rehospitalization and non-fatal events.

Statistical Analysis

Continuous variables are presented as means and standard deviations (SDs) or medians and interquartile ranges (IQRs). Categorical variables are presented as absolute values and percentages. A chi-square or Mann–Whitney–Wilcoxon test was employed to evaluate differences between the LLT and no LLT groups of each cohort. Multivariate logistic regression models were used to identify predictors of LDL-C target value attainment among LLT-treated patients. The covariates included in the models were age, gender, BMI, smoking status, hypertension, type 2 diabetes mellitus, stable angina, CKD, history of CHF, and statin dose. Kaplan–Meier analysis was used to assess mortality and non-fatal events in the ACS cohort at follow-up, with p-values calculated using a log-rank test. A p-value of <0.05 was considered statistically significant for all comparisons. SAS version 9.3 (Cary, NC, USA) was used for the statistical analyses.

RESULTS

Patients

A total of 612 patients were enrolled in the Vietnamese cohort of DYSIS II, 407 with stable CHD and 205 with an ACS.

The stable CHD cohort had a mean age of 65.0 years and 69.8% of the patients were male **(Table 1)**. Comorbidities and cardiovascular risk factors were common, in particular, hypertension (71.0%), type 2 diabetes mellitus (34.6%) and a sedentary lifestyle (18.3%). At the time of

Table 2: Patient characteristics - ACS

	All patients mean ± SD or % (n/N) (N = 205)	LLT mean ± SD or % (n/N) (N = 151)	No LLT mean ± SD or % (n/N) (N = 54)
Age (years)	65.9 ± 11.6	67.3 ± 11.6	62.1 ± 10.9
Male	69.3 (142/205)	68.9 (104/151)	70.4 (38/54)
BMI (kg/m^2)	22.7 ± 3.1	22.9 ± 3.3	22.3 ± 2.5
BMI > 30 kg/m^2	2.4 (5/205)	3.3 (5/151)	0.0 (0/54)
Comorbidities and CV risk factors			
Type 2 diabetes mellitus	21.1 (43/204)	23.3 (35/150)	14.8 (8/54)
Hypertension	61.5 (126/205)	65.6 (99/151)	50.0 (27/54)
CKD	5.4 (11/205)	6.6 (10/151)	1.9 (1/54)
History of stroke*	3.4 (7/204)	4.6 (7/151)	0.0 (0/53)
PAD	1.5 (3/204)	0.7 (1/151)	3.8 (2/53)
Current cigarette smoker	18.5 (38/205)	15.2 (23/151)	27.8 (15/54)
Sedentary lifestyle	19.5 (30/154)	20.0 (22/110)	18.2 (8/44)
Family history of CHD	0.5 (1/203)	0.0 (0/150)	1.9 (1/53)
ACS diagnosis			
STEMI/LBBB MI	20.0 (41/205)	11.3 (17/151)	44.4 (24/54)
NSTEMI	18.0 (37/205)	16.6 (25/151)	22.2 (12/54)
Unstable angina	62.0 (127/205)	72.2 (109/151)	33.3 (18/54)

Legend: *Includes ischemic and hemorrhagic stroke. BMI, body mass index; CV, cardiovascular; CHD, coronary heart disease; CKD, chronic kidney disease; LLT, lipid-lowering therapy; ACS, acute coronary syndrome; PAD, peripheral artery disease; STEMI, ST-segment elevation myocardial infarction; LBBB MI, myocardial infarction with left bundle branch block; NSTEMI, non-ST-elevation myocardial infarction. P-values calculated using chi-squared test or Mann–Whitney–Wilcoxon test.

the outpatient visit, 95.8% of patients were being treated with LLT. The demographic and clinical characteristics of patients did not vary significantly depending on whether or not they were being treated with LLT.

The mean age of the ACS cohort was 65.9 years and 69.3% were male **(Table 2)**. At the time of hospital admission, 73.7% of patients were being treated with LLT. The treated group was significantly older than the non-treated group (67.3 vs. 62.1 years; p < 0.01), and a higher proportion had hypertension (65.6% vs. 50.0%; p < 0.05). On the other hand, smoking was less common in the LLT group (15.2% vs. 27.8%; p < 0.05). The type of ACS also varied between groups, with a STEMI/LBBB MI being the diagnosis for a smaller proportion of the LLT-treated patients (11.3% vs. 44.4%; p < 0.0001).

Lipid profile

For the CHD cohort, the mean LDL-C level was calculated to be 90.5 ± 35.2 mg/dL, with the LLT-treated patients displaying a significantly lower value (89.2 ± 34.2 mg/dL) than those that were not treated (120.8 ± 44.1; p < 0.01) **(Table 3)**. The median values for HDL-C (43.0 vs. 38.0 mg/dL; p = 0.12) and triglycerides (117.0 vs. 210.0 mg/dL; p = 0.19) did not differ greatly between groups. The LDL-C target of <70 mg/dL had been achieved by 28.8% of the CHD patients overall, with this including 29.6% of the LLT group and 11.8% of the no LLT group (p = 0.11). The distance to this target for the two groups varied significantly, at 27.0 mg/dL for the treated patients and 55.0 mg/dL for those not treated. Female patients were less likely to have an LDL-C level below 70 mg/dL compared to males (OR: 0.557; 95% CI: 0.326–0.952); while no other variables included in the regression model had any predictive value **(Table 4)**.

The mean LDL-C level for the ACS cohort was 96.1 ± 43.4 mg/dL, with the LLT group having a lower level than the no LLT group (90.2 vs. 112.6 mg/dL, respectively; p < 0.01) **(Table 3)**. The median HDL-C levels did not vary between groups; however, triglycerides were significantly higher in the patients treated with LLT than in those that were not (165.0 vs. 132.5 mg/dL; p < 0.05). An LDL-C level of <70 mg/dL was recorded for 28.8% of the ACS patients overall, 33.8% of the LLT-treated patients and 14.8% of those not treated. The median distance to this value was similar for the two groups, however (31.0 and

Table 3. Lipid profile at baseline

	Stable CHD				ACS			
	All patients mean ± SD or median (IQR) or % (n/N) (N = 406)	LLT mean ± SD or median (IQR) or % (n/N) (N = 389)	No LLT mean ± SD or median (IQR) or % (n/N) (N = 17)	p-value (LLT vs. no LLT)	All patients mean ± SD or median (IQR) or % (n/N) (N = 205)	LLT mean ± SD or median (IQR) or % (n/N) (N = 151)	No LLT mean ± SD or median (IQR) or % (n/N) (N = 54)	p-value (LLT vs. no LLT)
LDL-C (mg/dL)	90.5 ± 35.2	89.2 ± 34.2	120.8 ± 44.1	<0.01	96.1 ± 43.4	90.2 ± 40.1	112.6 ± 48.2	<0.01
HDL-C (mg/dL)	43.0 (37.0, 50.0)	43.0 (37.0, 50.0)	38.0 (31.0, 45.0)	0.12	43.0 (35.0, 51.0)	43.0 (35.0, 51.0)	42.5 (35.0. 49.0)	0.43
Non-HDL-C (mg/dL)	188.0 (97.0, 146.0)	116.0 (95.0, 144.0)	154.0 (144.0, 208.0)	<0.0001	124.0 (94.0, 156.0)	119.0 (92.0, 154.0)	137.5 (103.0, 174.0)	<0.05
TC (mg/dL)	168.5 ± 41.3	166.7 ± 40.3	209.5 ± 44.6	<0.001	174.1 ± 49.4	170.1 ± 47.2	185.5 ± 53.8	<0.05
Triglycerides (mg/dL)	178.0 (125.0, 239.0)	177.0 (124.0, 236.0)	210.0 (145.0, 271.0)	0.19	151.0 (113.0, 215.0)	165.0 (115.0, 229.0)	132.5 (108.0, 172.0)	<0.05
LDL-C < 70 mg/dL*	28.8 (117/406)	29.6 (115/389)	11.8 (2/17)	0.11	28.8 (59/205)	33.8 (51/151)	14.8 (8/54)	<0.01
Distance to LDL-C < 70 mg/dL	27.0 (14.0, 50.0)	27.0 (13.0, 47.0)	55.0 (26.0, 100.0)	<0.01	35.0 (15.0, 61.0)	31.0 (15.0, 57.0)	40.0 (15.0, 80.0)	0.17

Legend: *Target for very high-risk patients.[10] HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol.

Table 4. Predictors for LDL < 70 mg/dL in patients treated with LLT

	Stable CHD		ACS*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age ≥ 70 years	0.768 (0.449–1.313)	0.334	1.016 (0.431–2.396)	0.970
Female	0.557 (0.326–0.952)	0.032	0.229 (0.080–0.653)	0.006
Obesity†	0.273 (0.033–2.289)	0.232	0.457 (0.042–5.007)	0.522
Current smoking	1.083 (0.474–2.472)	0.850	2.583 (0.700–9.535)	0.155
Stable angina	1.372 (0.841–2.237)	0.205	1.252 (0.420–3.730)	0.687
CKD	1.408 (0.679–2.919)	0.358	0.331 (0.052–2.104)	0.241
T2DM	1.102 (0.675–1.801)	0.698	0.898 (0.342–2.357)	0.828
History of CHF	1.062 (0.488–2.314)	0.879	2.843 (0.718–11.266)	0.137
Hypertension	1.020 (0.613–1.697)	0.940	1.345 (0.558–3.242)	0.509
Statin dose (>20 mg/day atorvastatin eq.)	1.000 (0.965–1.036)	0.997	0.952 (0.877–1.032)	0.233

Legend: *At hospital admission; †BMI >30 kg/m^2; CHF, congestive heart failure; CKD, chronic kidney disease; T2DM, type 2 diabetes mellitus

40.0 mg/dL for LLT and no LLT, respectively; p = 0.17). When the ACS patients were sub-divided according to pre-admission risk category, 62.9% were classed as being at very high-risk, 12.2% at high-risk, 21.5% at moderate risk and 2.4% at low risk **(Figure 1)**. The proportions of patients achieving their respective LDL-C targets decreased with increasing risk level, with only 28.7% of the very high-risk patients attaining a level of <70 mg/dL. Female LLT-treated patients were found to be less likely than males to achieve an LDL-C level below 70 mg/dL (OR: 0.229; 95% CI: 0.080–0.653; p = 0.006); while no other variables included in the regression model had any predictive value **(Table 4)**.

Use of lipid-lowering therapy

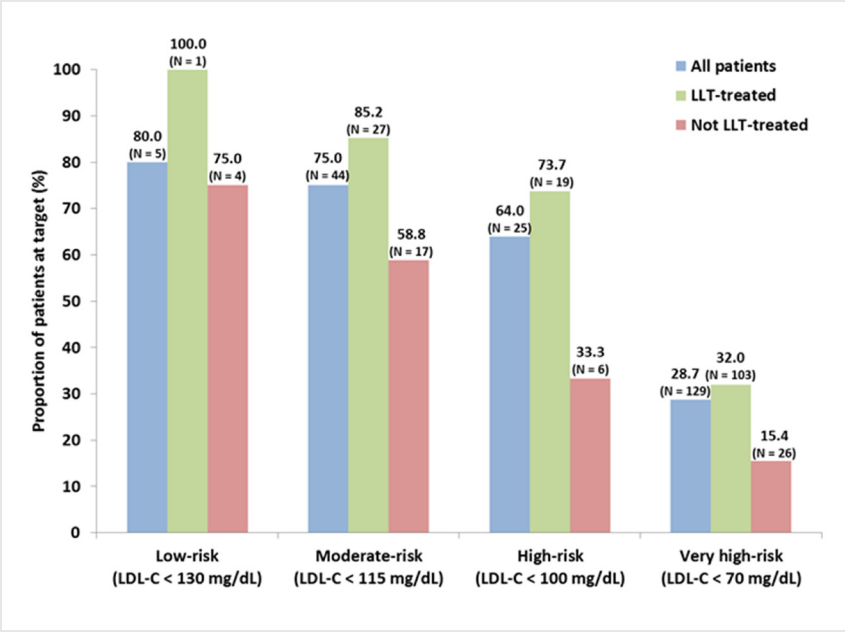
At the outpatient clinic visit, 95.8% of the stable CHD cohort was documented as being treated with LLT for at least 3 months at the time of visit **(Table 5)**. A statin was included as part of the therapy for 99.0% of these patients, with most (86.9%) taking it as monotherapy. The most commonly used statin was atorvastatin (52.8%), while rosuvastatin was prescribed for 35.0% and simvastatin for 10.9%. The mean atorvastatin-equivalent daily statin dosage was 15 ± 6 mg. A statin plus ezetimibe combination was being used by only 2.3% of the CHD patients. Use of other non-statins was higher, however, with 9.7% being treated with another non-statin in combination with a statin. Omega-3 fatty acids were the most commonly used of the non-statins (7.7% of the LLT-treated population), with fibrates also used (2.8%).

Table 5. Use of lipid-lowering therapy

	CHD	ACS	
	% (n/N) or mean ± SD (N = 407)	Admission % (n/N) or mean ± SD (N = 205)	4-month follow-up % (n/N) or mean ± SD (N = 205)
LLT	95.8 (390/407)	73.7 (151/205)	97.4 (186/191)
Statin therapy	99.0 (386/390)	98.0 (147/150)	100.0 (186/186)
Atorvastatin	52.8 (204/386)	47.6 (70/147)	48.4 (90/186)
Fluvastatin	0.0 (0/386)	0.0 (0/147)	0.0 (0/186)
Lovastatin	0.0 (0/386)	0.0 (0/147)	0.0 (0/186)
Pitavastatin	0.3 (1/386)	0.0 (0/147)	0.0 (0/186)
Pravastatin	0.0 (0/386)	0.0 (0/147)	0.0 (0/186)
Rosuvastatin	35.0 (135/386)	34.0 (50/147)	48.4 (90/186)
Simvastatin	10.9 (42/386)	1.4 (2/147)	1.1 (2/186)
Unknown	1.0 (4/386)	17.0 (25/147)	2.1 (4/186)
Statin daily dose – atorvastatin eq. (mg/day)*	15 ± 6	17 ± 5	18 ± 7
Statin monotherapy	86.9 (339/390)	91.3 (137/150)	97.8 (182/186)
Non-statin monotherapy	1.0 (4/390)	2.0 (3/150)	0.0 (0/186)
Statin + ezetimibe	2.3 (9/390)	0.7 (1/150)	0.5 (1/186)
Statin + other non-statin†	9.7 (38/390)	6.0 (9/150)	1.6 (3/186)

Legend: *Statin dosage normalized to atorvastatin potency.[11] †Includes fibrates, nicotinic acid and omega-3 fatty acids, with or without ezetimibe.

Figure 1: Target LDL-C attainment in ACS patients at baseline by pre-admission risk level



Legend: Risk levels and targets defined by ESC/EAS 2011 guidelines.[10] N refers to number of patients in each category.

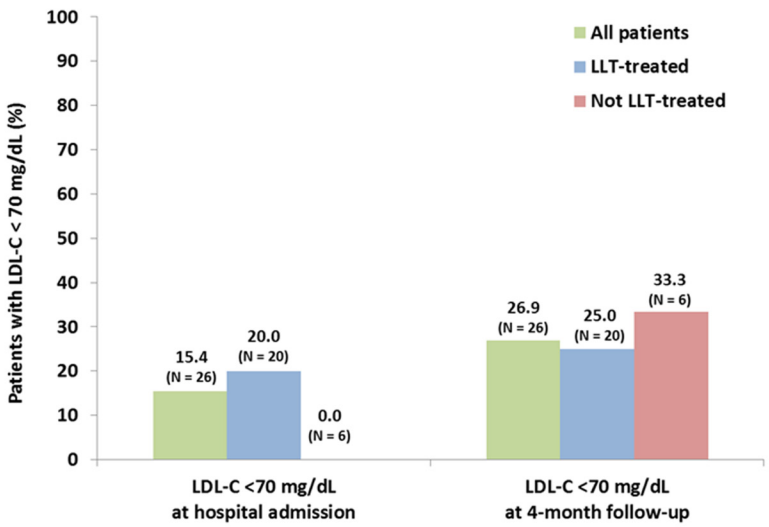
At admission to hospital, 73.7% of the ACS cohort was being treated with LLT **(Table 5)**. This included a statin in 98.0% of cases, with atorvastatin again the most commonly used (47.6%), followed by rosuvastatin (34.0%). The mean atorvastatin-equivalent daily statin dosage was 17 ± 5 mg. The majority of patients were taking the statin as monotherapy, with use of non-statins being extremely low.

At the 4-month follow-up interview, 97.4% of the ACS patients were being treated with LLT, all of whom were taking a statin as part of their treatment regimen. Statin use was split evenly between atorvastatin (48.4%) and rosuvastatin (48.4%). The mean daily statin dosage was similar to that calculated at baseline (18 ± 7 mg). Statin monotherapy was the LLT of choice for (97.8%) of patients, with non-statins used for only a small number of patients (2.2%).

Adverse cardiovascular events during follow-up for ACS cohort

Two patients died during the 4-month follow-up period, both from the group being treated with LLT prior to the index ACS. The Kaplan–

Figure 2: Achievement of LDL-C < 70 mg/dL at hospital admission and 4-month follow-up for ACS patients



Legend: Includes only patients with LDL-C levels available from both baseline and follow-up. N refers to number of patients in each category.

Meier mortality estimate was calculated to be 1.0% overall. No cardiovascular adverse events were documented during the follow-up period, although 4.1% of patients required rehospitalization.

DISCUSSION

Patients with stable or acute CHD in Vietnam displayed high levels of LDL-C, with few achieving the target that is recommended for reducing the risk of recurrent adverse events in such individuals. Many patients were being treated with LLT, in particular those with previously documented cardiovascular disease; however, the dosages of statins that were prescribed appeared to be insufficient. The data indicate a great need for improved monitoring and treatment of patients with cardiovascular disease in Vietnam.

The patients enrolled in both the CHD and ACS cohorts displayed low levels of obesity; however, other cardiovascular risk factors were common. Hypertension and type 2 diabetes mellitus in particular were highly prevalent. For the CHD cohort, there were no significant differences in baseline characteristics between the LLT-treated and not treated patients. In the ACS cohort, the LLT group appeared to have slightly greater proportions of patients with certain comorbidities than the no LLT group; however, only hypertension was significantly more common. Similar high rates of comorbidities have been previously reported for patients hospitalized with an acute MI in Vietnam.[12] Furthermore, with the rapid lifestyle changes occurring in the country, cardiovascular risk is set to increase to an even higher level.[2, 12]

It is therefore alarming that so few patients had an LDL-C value below the 70 mg/dL target for very high-risk individuals. The mean LDL-C level for the LLT-treated CHD patients was not much higher than the 70 mg/dL target; however, less than a third had attained this level. Target achievement was even lower for the non-treated patients, at only 11.8%. As all of these patients had previously diagnosed CHD, with many having suffered an ACS (15.5%) or having undergone PCI (70.3%), it appears that they were not being treated appropriately. Similar findings were reported by Park et al. for the Pan-Asian cohort of CEPHEUS, where only 34.9% of the very high-risk patients had achieved their target LDL-C level, despite all being treated with LLT (9). Although the value from this study compares favorably with the global cohort of CEPHEUS (22.8%),[8] it is still extremely poor.

In the ACS cohort, a higher proportion of the patients that were treated with LLT prior to hospitalization had an LDL-C level below 70 mg/dL (33.8%) compared to those who were not treated (14.8%). However, again, this is clearly sub-optimal, especially considering the high prevalence of cardiovascular risk factors documented for these patients. Indeed, 62.9% were classed as being at very high-risk, even before the ACS event, including almost half of the non-treated subjects. Target attainment was not much better at the follow-up point, reaching 26.9% overall. However, only 26 patients (12.7%) had their lipid levels re-checked during the 4 months after hospital discharge. The current ESC/EAS guidelines, and those available at the time of data collection, recommend that lipids should be tested 4–6 weeks after an ACS;[6, 10] therefore, it is possible that closer monitoring of patients could help to improve LDL-C target attainment.

Female patients in both the CHD and ACS cohorts were less likely than males to have an LDL-C level below 70 mg/dL at baseline. This is in agreement with data from the global CEPHEUS cohort[8] and the EUROASPIRE IV study.[13] Data from Asia specifically are varied, with target achievement being less likely for female hypercholesterolemic subjects in Hong Kong,[14] but more likely for their counterparts in Taiwan,[15] although these were both univariate analyses. In Korea, no association was found between gender and target attainment,[16] while in Indonesia, there were fewer females at target than males.[17] Such variation could be due to a number of factors, including incorporation of patients at all risk levels and different LDL-C targets; therefore, further evaluation of the effect of gender on LDL-C target attainment may be warranted.

The poor LDL-C target attainment identified in the Vietnamese patients of DYSIS II indicates that many patients are receiving inadequate treatment although the recommendation on the management of dyslipidemia by National Heart Association insisted on LDL-C target of < 70mg/dL on very high risk patients.[28] Being an inclusion criterion, all of the patients in the CHD cohort had known cardiovascular disease, yet some were not being treated with LLT and for those that were, the mean statin dosage was low. Furthermore, there was little use of statin plus non-statin combination therapy. At admission to hospital, almost three quarters of the ACS patients were being treated with LLT; however, again, the mean statin dosage was extremely low, and use of non-statins was rare. At the 4-month follow-up, most of the patients that were not being treated with LLT prior to the ACS event were receiving such therapy. This is partially in accordance with European guidelines, which recommend that patients that have suffered an ACS should be treated with high-dose statin therapy within the first 1–4 days after the event.[10] However, the mean daily statin dosage was low and use of combination therapy had actually decreased from baseline, indicating a lack of treatment maximization. High use of statins after an ACS was also demonstrated by Nguyen et al. in a retrospective analysis of patients in Vietnam.[18] They found that 94.1% of ACS patients were treated with statin therapy in the 24 h after hospital admission; however, they did not report the dosages used.

The benefits of lowering LDL-C levels with LLT are well-established, with more intensive therapy having been shown to result in superior outcomes.[19, 20] Furthermore, the addition of ezetimibe to statin therapy has been shown to have superior LDL-C lowering ability compared to use of the same statin alone,[21] or to the use of double the dose of the statin.[22] The low statin dosages and scarce use of combination therapy in the present study indicate a significant level of under-treatment of these very high-risk patients. One reason for this may be the increasing risk of side-effects with higher doses of statins, yet in reality, these are quite rare.[23, 24] There is also a perception that high-dose statins may not be safe for Asian patients; however, an analysis of 58 trials of atorvastatin identified few differences in adverse events between Asians and non-Asians.[25] A further potential reason for the low doses of statins used in the Vietnamese patients included in DYSIS II is the knowledge that the pharmacokinetics of statins vary between Asians and non-Asians. It has been shown that statin exposure is higher in Asians than in Caucasians,[26] and that a lower statin dosage is required for Asians to achieve similar LDL-C-lowering to Westerners.[27] The low dosages of statins used in the present study may be an indication that physicians are not adequately titrating the drugs in response to measured lipid levels.

The main limitation to the present study is that few of the ACS patients had their lipid levels re-checked after discharge from hospital. Although this highlights a deficiency in the monitoring of such individuals, it also makes it difficult to evaluate any associations between lipid levels, LLT use and cardiovascular outcome. Furthermore, the occurrence of adverse events during follow-up was too low to enable comparisons to be made between groups. For the CHD cohort, the imbalance in group size decreased the accuracy of any comparisons between LLT-treated and not treated patients; however, this was reflective of LLT use in real-world clinical practice in Vietnam.

CONCLUSIONS

Hyperlipidemia was highly prevalent in patients with stable or acute CHD in Vietnam. Few patients had achieved guideline-recommended LDL-C levels, despite widespread use of LLT. The data indicate that this LLT was not optimized in most cases, with low doses of statins used and combination therapy rarely employed. Furthermore, in the ACS cohort, monitoring of lipid levels after the index event was extremely poor. In order to reduce the risk of recurrent cardiovascular events in these patients, more frequent lipid testing and subsequent intensification of LLT is essential.

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