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Low-density lipoprotein cholesterol target achievement in patients surviving an acute coronary syndrome in Hong Kong and Taiwan - findings from the Dyslipidemia International Study II☆

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ABSTRACT

Background: Individuals are at increased risk for cardiovascular events following an acute coronary syndrome (ACS). Effective management of hyperlipidemia, an associated risk factor, is essential for improving outcomes. We aimed to quantify the extent of hyperlipidemia and its treatment in ACS survivors in Hong Kong and Taiwan.
Methods: The multinational, observational Dyslipidemia International Study (DYSIS) II included patients hospitalized for an ACS. Lipid levels and use of lipid-lowering therapy (LLT) were evaluated at baseline and 4 months post-discharge. The proportions of patients attaining the recommended LDL-C target for individuals at very high cardiovascular risk (<70 mg/dL) was assessed and potential predictors of this outcome evaluated.
Results: In total, 270 patients were enrolled, 125 (46.3%) of which were being treated with LLT prior to hospitalization. Of these, 28.8% had an LDL-C level < 70 mg/dL, compared to only 6.9% of those not being treated. Statin monotherapy was the most commonly employed LLT, with a mean atorvastatin-equivalent dosage of 14 mg/day. By 4-month follow-up, target attainment had risen to 45.1% for patients treated with LLT at baseline, and 43.3% for those who had not been treated. LLT was being used by 88.4% of patients at follow-up, with a mean atorvastatin dosage of 18 mg/day. Use of statins in combination with ezetimibe/other non-statin was scarce. No predictors of LDL-C target attainment were identified.
Conclusions: In patients hospitalized with an ACS, rates of LDL-C target achievement were poor. While LLT was widely employed, statin intensity was low and combination therapy underused, indicating scope for improvement.

1. Introduction

Coronary heart disease (CHD) has been estimated to cause approximately 8.8 million deaths in 2015, making it the leading cause of mortality globally [1]. Patients with CHD are at risk of recurrent adverse cardiovascular events, including acute coronary syndrome (ACS). In the Asia–Pacific region, ACS has become a common cause of death, with around half of the global burden of cardiovascular mortality located in this area [2,3]. It is, therefore, essential that the risk factors associated with CHD are effectively managed in this population [4,5].

One such risk factor is hyperlipidemia, with every 39 mg/dL (1 mmol/L) increase in total cholesterol (TC) raising the risk of coronary death by around 35% [6]. Strategies to lower cholesterol primarily focus on reducing levels of low-density lipoprotein cholesterol (LDL-C). This has been shown to significantly lower the probability of a major cardiovascular event [7]. Evidence-based guidelines from the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) advocate a value of <70 mg/dL for patients that have suffered an ACS, with less strict targets for individuals at lower cardiovascular risk [8]. However, attainment of these targets has been shown to be extremely poor, despite widespread use of lipid-lowering-therapy (LLT). In the Centralized Pan-Regional Survey on the Undertreatment of Hypercholesterolemia (CEPHEUS) study, only 22.8% of the very high-

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risk LLT-treated patients in the global cohort had achieved their LDL-C target [9]. In the Pan-Asian population, goal attainment was slightly higher at 34.9%, with Hong Kong displaying a vastly superior value of 83.1% [10].

There is a variety of pharmacological treatments available for lowering LDL-C, the most common being statins and the cholesterol absorption inhibitor, ezetimibe. In patients that have suffered an ACS, guidelines recommend prompt initiation of intensive LLT [8,11]. However, studies in Hong Kong and Taiwan found rates of statin use to be only 74.1% and 60.5%, respectively, for patients being discharged from hospital after an ACS [12,13]. Therefore, it appears that LLT is not being used to its full potential in these very high-risk subjects.

The multinational Dyslipidemia International Study (DYSIS) II was performed in order to quantify the extent of hyperlipidemia in patients with stable or acute CHD across the world. The present study concerns subjects from Hong Kong and Taiwan who had been hospitalized due to an ACS. We aimed to evaluate LDL-C target attainment, as well as to elucidate the strategies being used to treat hyperlipidemia in such very high-risk patients.

2. Methods

2.1. Study design

Patients were enrolled in DYSIS II from 17 institutions across Hong Kong and Taiwan from December 2013 to August 2014. Subjects were included if they were being hospitalized due to an ACS, were over 18 years of age, and had a full lipid profile measured within 24 h of admission. An ACS was defined as an ST-segment elevation myocardial infarction (STEMI) or left bundle branch block myocardial infarction (LBBB MI), a non-ST-segment elevation myocardial infarction (NSTEMI), or unstable angina (UA). Patients that did not survive until hospital discharge were excluded, as were those that were participating in a clinical trial at the time of the study. Data were collected at hospital admission and at a telephone interview 4 months (±15 days) post-admission. Patients were divided according to whether or not they were being treated with LLT prior to the index ACS. Treatment duration was required to be at least three months for the patient to be included in the LLT group.

The study protocol and its amendments were approved by the country-specific local ethics review committees and the study was performed in accordance with the Declaration of Helsinki and Good Clinical Practice (ICH-GCP). All subjects provided written informed consent to participate.

2.2. Documentation

Data were collected using the web-based data collection software EBogen©, developed by the Institut für Herzinfarktforschung (IHF) in Ludwigshafen, Germany. At hospital admission, demographic and clinical variables were recorded, including age; gender; race/ethnicity; body mass index (BMI); lifestyle factors, including a sedentary lifestyle and smoking habits; presence of hypertension, diabetes mellitus, congestive heart failure (CHF), chronic kidney disease (CKD), or peripheral artery disease (PAD); previous myocardial infarction (MI) or stroke; documentation of CHD; or a family history of CHD. A patient was considered obese if they had a BMI of >30 kg/m^2. Hypertension was defined as a previous diagnosis, current antihypertensive medication, or a blood pressure of >140/90 mmHg. Diabetes was defined as a previous diagnosis, current antidiabetic treatment, or a fasting blood glucose level of ≥126 mg/dL. A sedentary lifestyle was defined as <20–30 min of walking on fewer than 3–4 days per week.

Pre-admission cardiovascular risk status was defined according to the 2011 ESC/EAS guidelines as very high, high, moderate or low, with corresponding LDL-C targets of <70 mg/dL, <100 mg/dL, <115 mg/dL and <130 mg/dL, respectively [14]. All patients were classified as very high-risk at the point of admission on the basis of the qualifying ACS event. Serum levels of TC, LDL-C, high density lipoprotein cholesterol (HDL-C), non-HDL-C, and triglycerides were measured for each patient. The LLT which patients were taking prior to hospital admission and at the 4-month follow-up interview was documented, including statin monotherapy, non-statin monotherapy, statin plus ezetimibe, and statin plus other non-statin (nicotinic acid, fibrates, omega-3 fatty acids). The statins assessed were atorvastatin, simvastatin, rosuvastatin, fluvastatin, lovastatin, pravastatin and pitavastatin. Statin dosages were normalized to atorvastatin potency in order to allow comparisons between patients to be made. These dose equivalents were based on clinical trial data comparing the LDL-C-lowering efficacy of the different statins [15].

At the 4-month follow-up, the occurrence of any adverse events since hospital discharge was documented. The specific LLT that each patient was being treated with was also recorded, along with any lipid profiles that were collected during the follow-up period.

2.3. Statistical analysis

Data are reported as means with standard deviations (SD), medians with interquartile ranges (IQR), or absolute values with percentages. Statistical significance was determined using the chi-squared test or the Mann–Whitney–Wilcoxon test. LDL-C target achievement was assessed at hospital admission and follow-up.

For the patients treated with LLT prior to hospital admission, multivariable logistic regression was used to identify variables predictive of achievement of an LDL-C level of <70 mg/dL. Age, female gender, obesity, current smoking, sedentary lifestyle, stable angina, CKD, type 2 diabetes mellitus, history of CHF, hypertension, and statin dose (i.e., atorvastatin dose equivalent) were selected as covariates.

SAS version 9.3 (Cary, NC, USA) was used for all the statistical analyses, with a p-value of <0.05 considered statistically significant.

3. Results

3.1. Patients

A total of 270 patients being hospitalized with an ACS were included in the pooled Hong Kong and Taiwan cohort of DYSIS II. Their mean age was 64.4 years and 76.3% were male (Table 1). Of these, 125 (46.3%)

Table 1
Demographic and clinical characteristics of ACS patients.

	All patients % (n/N) or mean ± SD (N = 270)	LLT-treated % (n/N) or mean ± SD (N = 125)	Not LLT-treated % (n/N) or mean ± SD (N = 145)	p-value
Age (years)	64.4 ± 11.9	68.2 ± 10.8	61.1 ± 11.8	<0.0001
Male	76.3 (206/270)	68.0 (85/125)	83.4 (121/145)	<0.01
BMI > 30 kg/m^2	8.9 (24/270)	9.6 (12/125)	8.3 (12/145)	0.70
Comorbidities & cardiovascular risk factors				
Hypertension	65.2 (176/270)	85.6 (107/125)	47.6 (69/145)	<0.0001
Type 2 diabetes mellitus	39.2 (105/268)	54.8 (68/124)	25.7 (37/144)	<0.0001
Documented CHD	32.2 (84/261)	54.2 (65/120)	13.5 (19/141)	<0.0001
Prior MI	18.8 (49/260)	34.5 (41/119)	5.7 (8/141)	<0.0001
Prior stroke (ischemic or hemorrhagic)	8.3 (22/266)	13.1 (16/122)	4.2 (6/144)	<0.01
CKD	10.0 (27/270)	14.4 (18/125)	6.2 (9/145)	<0.05
PAD	4.5 (12/269)	7.2 (9/125)	2.1 (3/144)	<0.05
Sedentary lifestyle	40.4 (107/265)	46.7 (57/122)	35.0 (50/143)	0.05
Current smoker	26.7 (72/270)	16.0 (20/125)	35.9 (52/145)	<0.001
Family history of CHD	26.7 (68/255)	24.4 (29/119)	28.7 (39/136)	0.44
Type of ACS when admitted to hospital				
STEMI/LBBB MI	32.6 (88/270)	20.8 (26/125)	42.8 (62/145)	<0.001
NSTEMI	44.4 (120/270)	40.8 (51/125)	47.6 (69/145)	0.26
Unstable angina	23.0 (62/270)	38.4 (48/125)	9.7 (14/145)	<0.0001

Legend: ACS, acute coronary syndrome; CHD, coronary heart disease; CKD, chronic kidney disease; CRF, chronic renal failure; LBBB, left bundle branch block; LLT, lipid-lowering therapy; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; BMI, body mass index. P-values calculated using chi-square or Mann-Whitney-Wilcoxon tests between values for treated and not treated patients.