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Cholesterol target value attainment and lipid-lowering therapy in patients with stable or acute coronary heart disease: Results from the Dyslipidemia International Study II

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ABSTRACT

Background and aims: Low-density lipoprotein cholesterol (LDL-C) is a major contributor to cardiovascular disease. In the Dyslipidemia International Study II (DYSIS II), we determined LDL-C target value attainment, use of lipid-lowering therapy (LLT), and cardiovascular outcomes in patients with stable coronary heart disease (CHD) and those suffering from an acute coronary syndrome (ACS).
Methods: DYSIS II included patients from 18 countries. Patients with either stable CHD or an ACS were enrolled if they were ≥18 years old and had a full lipid profile available. Data were collected at a physician visit (CHD cohort) or at hospital admission and 120 days later (ACS cohort).
Results: A total of 10,661 patients were enrolled, 6794 with stable CHD and 3867 with an ACS. Mean LDL-C levels were low at 88 mg/dl and 108 mg/dl for the CHD and ACS cohorts respectively, with only 29.4% and 18.9% displaying a level below 70 mg/dl. LLT was utilized by 93.8% of the CHD cohort, with a mean daily statin dosage of 25 ± 18 mg. The proportion of the ACS cohort treated with LLT rose from 65.2% at admission to 95.6% at follow-up. LLT-treated patients, who were female, obese, or current smokers, were less likely to achieve an LDL-C level of <70 mg/dl, while those with type 2 diabetes, chronic kidney disease, or those taking a higher statin dosage were more likely.
Conclusions: Few of these very high-risk patients achieved the LDL-C target, indicating huge potential for improving cardiovascular outcome by use of more intensive LLT.

1. Introduction

Cardiovascular disease, including both ischemic coronary heart disease (CHD) and stroke, has become the leading cause of death

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worldwide [1]. Ischemic heart disease arises from occlusion of the coronary arteries, which results in reduced blood flow to the heart, damage to the cardiac tissue, and, potentially, death. Arterial occlusion is most often caused by the gradual accumulation of lipoproteins and foam cells in the vessel wall, initiating an inflammatory cascade and a build up of atherosclerotic plaque. Acute coronary syndrome (ACS) is a severe and life-threatening clinical manifestation of cardiovascular disease, which is characterized by a sudden reduction in blood flow to the heart as a result of plaque rupture.

The benefits of LDL-C lowering via statin treatment, especially early after an ACS, have been established [2–7]. Despite the evidence of the benefits to patients with stable and acute CHD of lowering this type of cholesterol, attainment of the recommended LDL-C levels is not well characterized [8]. Several reports from the Dyslipidemia International Study (DYSIS) assessed achievement of LDL-C targets in statin-treated patients, and reported attainment of a level of <70 mg/dl ranging from 14% to 40% for the very high-risk patients [9–12]. Furthermore, in EUROASPIRE IV, a cross-sectional study of European patients with a first or recurrent coronary event, just 17.5% of patients on a low/moderate-intensity lipid-lowering therapy (LLT) regimen and 26.6% of patients on a high-intensity LLT regimen had an LDL-C level of <70 mg/dl [13]. However, no other international studies have assessed the rates of LDL-C target value attainment in both stable and acute CHD patients. Thus, DYSIS II was carried out to assess the frequency and predictors of LDL-C target achievement in multiple regions across the globe. Treatment with statin and non-statin LLT was also documented, and outcomes were compared across regions to provide insight into the management of stable CHD and ACS in various parts of the world.

2. Patients and methods

2.1. Study design

DYSIS II was a multinational, multicenter, prospective observational study of lipid profiles, lipid target value attainment, and LLT in patients with stable CHD and in patients being hospitalized for an ACS event. From 2012 to 2013, patients were enrolled from eighteen countries in Asia (Hong Kong, India, South Korea, the Philippines, Singapore, Thailand, Taiwan, and Vietnam), Europe (France, Greece, Germany, Ireland, and Italy), and the Middle East (Egypt, Jordan, Lebanon, Saudi Arabia, and the United Arab Emirates). All data were collected via a web-based data collection form using software developed by the Institut für Herzinfarktforschung in Ludwigshafen, Germany.

Acute care centers and site investigators were selected to be representative of the acute and ambulatory treatment of secondary prevention in the participating countries (this varied from country to country due to differences in health care systems). Study enrollment was designed to include a representative cohort of patients being treated with LLT at the time of the physician visit (CHD cohort) or at hospital admission for the ACS.

Data were collected by clinical examination and from medical charts. For the ACS cohort, data were collected at admission and discharge from the hospital, and again via a telephone interview at 120 ± 15 days after admission (the follow-up time point) (Supplementary Fig. 1).

The study protocol was approved by national and regional ethics committees according to local regulations, and was performed in accordance with the declaration of Helsinki. All patients provided written informed consent.

2.2. Patients

Patients included in DYSIS II were aged ≥18 years and were either attending a scheduled physician visit for stable CHD (CHD cohort) or were being hospitalized due to an ACS (ACS cohort). Stable CHD was defined as one or more of the following: coronary stenosis of >50%, as assessed by coronary angiography or cardiac CT; prior percutaneous coronary intervention (PCI); prior coronary artery bypass grafting (CABG); or a history of ACS (>3 months prior to enrolment). 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. Patients were required to have a full lipid profile available. For the CHD cohort this was from within the 12 months prior to the appointment. For the ACS cohort, this was constructed from blood taken during the first 24 h after hospital admission. ACS patients that did not survive until discharge were excluded, as were any individuals taking part in a clinical trial at the time of the DYSIS II study.

2.3. Documentation and definitions

Demographic and clinical variables collected at baseline included age, gender, ethnicity, body mass index (BMI), sedentary lifestyle, smoking status, a family history of CHD, and comorbidities such as hypertension, type 2 diabetes mellitus, history of myocardial infarction (MI), chronic kidney disease (CKD) or chronic renal failure (CRF), stroke, or peripheral vascular disease. Obesity was defined as BMI >30 kg/m^2 according to the World Health Organization guidelines. Diabetes was defined as current treatment for diabetes, a previous diagnosis of diabetes, or a fasting plasma glucose level of ≥126 mg/dl. Likewise, hypertension was defined as current treatment, a previous diagnosis, or having blood pressure >140/90 mmHg. A sedentary lifestyle was defined as <20–30 min of walking on <3–4 days per week. Stroke could be ischemic or hemorrhagic.

The lipid profile included measurement or calculation of serum levels of total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), non-HDL-C, and triglycerides, as per local practice. Achievement of LDL-C target levels, as defined in the ESC/EAS guidelines [14], was determined for both cohorts. For the CHD cohort, all patients were classed as being at very high risk, and therefore had an LDL-C target of <70 mg/dl. For the ACS cohort, pre-ACS cardiovascular risk status was determined according to the ESC/EAS guidelines [14], and targets for LDL-C for very high-risk, high-risk, moderate-risk, and low-risk patients were defined as <70 mg/dl, <100 mg/dl, <115 mg/dl, and <130 mg/dl, respectively. LDL-C goal attainment by risk status was based on the lipid values determined from blood taken within 24 h of hospital admission, which reflected lipid levels from the pre-ACS period. As the occurrence of the ACS placed all patients into the very high-risk category, attainment of LDL-C < 70 mg/dl was also calculated. The median distance to the LDL-C target was calculated for patients who had not attained this level on the date of the lipid profile.

Patients were divided into subgroups based on whether or not they were being treated with LLT at baseline. For the ACS cohort, the designations of ‘treated’ or ‘on LLT’ refer to the treatment status immediately prior to hospital admission, regardless of whether treatment was still ongoing at follow-up. The following mutually exclusive classes of LLT were assessed: statin monotherapy, non-statin monotherapy, statin plus ezetimibe, and statin plus other non-statin therapy (‘other’ non-statins included fibrates, omega-3 fatty acids, and nicotinic acid). The statins assessed were atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin. Atorvastatin dose equivalents were based on