Attainment of low-density lipoprotein cholesterol target in patients with coronary heart disease: still a long way to go

Kornelia Kotseva\textsuperscript{a,b}

\textsuperscript{a} National Heart & Lung Institute, Imperial College London, UK
\textsuperscript{b} Department of Public Health, Ghent University, Belgium

Corresponding author:
Kornelia Kotseva
National Heart & Lung Institute, Imperial College London
Emmanuel Kaye Building, Royal Brompton Hospital Campus
1b Manresa Road, London SW3 6LR, UK
E mail: k.kotseva@imperial.ac.uk

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Kornelia Kotseva

Despite major progress in the diagnosis and treatment, cardiovascular disease (CVD) remains a leading cause of death, premature disability and increasing health care costs worldwide. According to the World Health Organization, of the 56.4 million deaths in 2015, CVD accounted for 15 million, around 7.4 million from coronary heart disease (CHD) and 6.7 million following stroke. [1] While many developed countries have seen recently a decline in cardiovascular mortality rates, no such improvement was found in lower income countries with the Asia-Pacific region accounting for approximately half of the burden of CVD globally.[2] This is due to the demographic changes and the urbanization, but also increased tobacco smoking, poorer diet, more sedentary lifestyle and increased prevalence of obesity that has led to an increasing prevalence of hypertension, dyslipidaemia, and diabetes mellitus.

The 2011 and 2016 European Society of Cardiology and the European Atherosclerosis Society (ESC/EAS) guidelines of the management of dyslipidaemia recommend that the LDL cholesterol target for patients at very high cardiovascular risk should be < 70 mg/dL (< 1.8 mmol/L). [3,4] However, many studies have reported very poor lipid management in patients with atherosclerotic heart disease throughout the world.[5-10] The observational, cross-sectional, multinational Dyslipidemia International Study (DYSIS) II was established to quantify the extent of hyperlipidemia in patients with stable or acute coronary heart disease globally and to analyze the predictors of lipid target achievement. [5,6]

In this issue of the EJPC Kian-Keong Poh and co-authors present the DYSIS II data from nine countries in the Asia-Pacific region (Hong Kong, India, Indonesia, the Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam) that participated in this global study.[11] A total of 4592 patients were enrolled from July 2013 to October 2014 at the outpatient appointment for stable CHD or at hospital admission for acute coronary syndrome (ACS). To be eligible all patients were required to have a full lipid profile available from the most recent blood test within the 12 months prior to enrollment (CHD cohort) or from blood taken during the first 24 hours after hospital admission (ACS cohort). The duration of treatment in the lipid-lowering therapy (LLT) groups should had been 3 months or longer. The objective was to assess the lipid-lowering therapy and low-density lipoprotein (LDL) cholesterol target attainment (<70mg/dL) as recommended in the ESC/EAS lipid guidelines for very high-risk patients.[4] For the acute coronary syndrome cohort any fatal or non-fatal adverse events were recorded at the 4-month follow-up.

The results showed poor lipid management of patients with stable coronary disease or ACS in Asia, with a minority achieving the LDL cholesterol targets set out in evidence-based guidelines. The use of LLTs and monitoring of lipid levels in both groups were inadequate. Despite the majority of patients being at very high risk of cardiovascular events, mean LDL cholesterol levels were high in both groups, higher in the ACS cohorts than in the stable CHD cohort (103 mg/dL and 87 mg/dL, respectively).
The use of lipid-lowering therapies was higher in the stable CHD cohort (92%) than in the ACS cohort (63%). In the stable CHD patients, only 13% of those not treated with LLT had reached the recommended target. While target achievement was higher for the treated patients, it was still only 33%. Poor LDL cholesterol target achievement was also evident for the ACS cohort, with LDL cholesterol levels even higher than for the stable CHD cohort in both the LLT-treated and non-treated groups. Target attainment was significantly higher in lipid-lowering therapy treated (31%) than non-treated patients (9%). It decreased with increasing pre-admission risk level, with less than a quarter of the very high-risk patients achieving their recommended target. Less than a third (30%) of ACS patients had a repeat lipid test during the follow-up period. Although LDL cholesterol target attainment had improved after discharge, only two-fifths (42%) of patients achieved LDL cholesterol <70mg/dL during the follow-up.

The DYSIS II results are in accordance with other multinational surveys in the Asia-Pacific region, Europe and throughout the world showing poor management and under treatment with major geographical variations in the control of LDL cholesterol in many regions of the world.[5-10] These variations may be due to the different populations being investigated in different studies. The results of EUROASPIRE IV survey demonstrated low rates of achieving LDL-cholesterol target in patients with CHD from 24 countries in Europe. [7] Overall, 87% of coronary patients were on lipid-lowering therapy at least six months after their recruiting coronary event and only one fifth of them had LDL cholesterol of < 70 mg/dL. The SURF international clinical audit on cardiovascular risk factor control in 11 countries reported that the LDL-cholesterol goal was achieved by 30%, with better target attainment in Europe (33%) than in Asia (15%). [8] In the DYSIS study, only 22% of patients (24% in Asia/China) being at very high risk were documented to achieve their target of LDL cholesterol < 70mg/dL [5] Similar findings were reported in the Centralized Pan-regional Surveys on the Undertreatment of Hypercholesterolaemia (CEPHEUS) with LDL-cholesterol goal being achieved by 23% (35% of Asian patients).[10]

The DYSIS II results in Asia-Pacific region showed that the LDL cholesterol target achievement was associated with a number of factors. Female LLT treated patients were less likely to achieve the LDL cholesterol target than men in both stable CHD and ACS groups. This finding has been reported previously elsewhere and confirms some observations that women are less likely to receive evidence-based treatment than men. Other interesting findings were that patients with diabetes mellitus type 2 were more likely to achieve the LDL cholesterol goal in the stable CHD group, while the older age in the ACS group was associated with better attainment of LDL cholesterol target in LLT treated patients.

The proportions of patients who achieved the LDL cholesterol target varied across the countries and ethnic groups with higher proportions of Indian and Korean patients achieving the LDL cholesterol of <70mg/dL. This may be related to differences in clinical practice, different guidelines and genetic factors.

Although it is clear that in the DYSIS II Asia-Pacific study LLT was associated with a reduction in LDL cholesterol levels, the poor target attainment indicates that the medication was not used effectively. The 2016 EAS/ESC guidelines advocate, irrespective of LDL cholesterol level, prescription of lipid-lowering medications in all patients with documented CHD and initiation of high-dose statins early after ACS, if not
contraindicated. [4] High-intensity statins such as atorvastatin 80 mg or rosuvastatin 20-40 mg have been shown to provide LDL cholesterol reduction of up to 60%. In the DYSIS II Asia-Pacific study, despite the high use of LLT only about a third of patients in the LLT-treated group had achieved their target for LDL cholesterol. Explanations for inadequate lipid control may include starting with a low dose statins and not up-titrating, not using a combination of drug therapies, and poor patient adherence. The monitoring of patients after discharge was inadequate with less than a third of ACS patients having further lipid profile available at the 4-month follow-up. The mean atorvastatin-equivalent daily statin dosage was low, calculated to be only 20 mg/day for the stable CHD group and 27 mg/day for ACS group. The reasons for prescribing the suboptimal statin dosages may include a fear of adverse effects, however recent studies on safety of even very low levels of LDL cholesterol showed that statins should be prescribed on their maximum tolerated dose in almost all patients with CHD. Another contributing factor could be the evidence from some studies that Asians require lower statin dosages than non-Asians. Furthermore, very few patients were treated with combinations of statin and non-statin medications that may be cost-related or due to different local health insurance systems. Most of the international guidelines are mainly based on Western populations and their applicability to people in Asia is largely untested. Only recently, a number of Asian countries have published their own guidelines for the treatment of dyslipidaemia and that should improve the lipid management in this region of the world. It is well known that unhealthy lifestyles have adverse impact on the control of major CVD risk factors including raised LDL-cholesterol. That is why it is important that the guidelines include also country-specific dietary recommendations adapted to local foot habits and socio-economic differences.

The results of the DYSIS II study demonstrate that there is a wide treatment gap between the evidence based guidelines and everyday clinical practice in patients with stable or acute CHD in Asia. It is clear that much more has to be done to improve the lipid management in these patients with effective lifestyle interventions, and by using high intensity statins and combination LLTs, and improving patient and physicians adherence. Secondary prevention needs comprehensive, multidisciplinary lifestyle and therapeutic management and local guidelines adapted to the cultural settings in each country in order to reduce the risk of future cardiovascular events in patients with CHD.

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