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Prevalence of Lipid Abnormalities and Cholesterol Target Value Attainment in Patients with Stable and Acute Coronary Heart Disease in the United Arab Emirates

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Abstract

Background:

Careful management of lipid abnormalities in patients with coronary heart disease (CHD) or an acute coronary syndrome (ACS) can reduce the risk of recurrent cardiovascular events. The extent of hyperlipidemia in these very high-risk patients in the United Arab Emirates (UAE), along with the treatment strategies employed, is not clear.

Methods:

The Dyslipidemia International Study II was a multinational observational analysis carried out from 2012 to 2014. Patients were enrolled if they had either stable CHD or an ACS. Patient characteristics, lipid levels, and use of lipid-lowering therapy (LLT) were recorded at enrollment. For the ACS patients, the LLT used during the 4 months' follow-up period was documented, as were any cardiovascular events.

Results:

A total of 416 patients were recruited from two centers in the UAE, 216 with stable CHD and 200 hospitalized with an ACS. Comorbidities and cardiovascular risk factors were extremely common. A low-density lipoprotein cholesterol level of <70 mg/dl, recommended for patients at very high cardiovascular risk, was attained by 39.3% of the LLT-treated CHD patients and 33.3% of the LLT-treated ACS patients at enrollment. The mean atorvastatin-equivalent daily statin dose was 29 ± 15 mg for the CHD patients, with 13.7% additionally using ezetimibe. For the ACS patients, the daily dosage was 23 ± 13 mg at admission, rising to 39 ± 12 mg by the end of the 4-month follow-up. The use of nonstatin agents was extremely low in this group.

Conclusions:

Despite LLT being widely used, hyperlipidemia was found to be prevalent in ACS and CHD patients in the UAE. Treatment strategies need to be significantly improved to reduce the rate of cardiovascular events in these very high-risk patients.

Keywords: Cholesterol, coronary artery disease, dyslipidemia, lipids, statins

INTRODUCTION

Cardiovascular disease is a growing problem throughout the world. In 2010, 29% of deaths in the United Arab Emirates (UAE) were caused by this condition.[1] Individuals with coronary heart disease (CHD) are at very high risk for suffering recurrent cardiovascular adverse events, both fatal and nonfatal. In order to improve the outcome for these patients, management of associated risk factors such as diabetes mellitus, hypertension, and dyslipidemia is of paramount importance. In the UAE, these comorbidities are highly prevalent in the general population and found to an alarming extent in younger people.[2,3,4] This had led to the control of cardiovascular risk factors being the number one health-care priority in the UAE.[1,5]

The treatment of hyperlipidemia with the use of lipid-lowering therapy (LLT) such as statins has been shown to be highly effective for improving cardiovascular health.[6,7,8] Reducing levels of low-density lipoprotein cholesterol (LDL-C) in particular are the major focus of strategies to prevent and slow the progression of CHD.[9,10,11] Indeed, it has been demonstrated that lowering LDL-C levels by around 39 mg/dl (1 mmol/l) could reduce the 5-year occurrence of major vascular events by approximately a fifth.[6] The most recent guidelines from the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) advocate an LDL-C level of <70 mg/dl (1.8 mmol/l) for patients at very high cardiovascular risk, such as those with established CHD and other comorbidities.[10] However, despite treatment with LLT, the majority of patients have failed to attain this goal. In the first Dyslipidemia International Study (DYSIS), of the 30 countries involved, the UAE and Kuwait combined were found to have the highest proportion of very high-risk statin-treated patients with an LDL-C level below 70 mg/dl (44.9%).[12] In comparison, the Middle East and Africa region as a whole had a value of 26.6%, with the lowest target achievement being for Spain at only 10.1%.[12,13] In the Centralized Pan-Middle East Survey on the under-treatment of hypercholesterolemia (CEPHEUS), the Arabian Gulf countries, which included the UAE, it was found that 31.9% of very high-risk patients had an LDL-C level of <70 mg/dl,[14] while only 24.8% of the Levant cohort were at goal.[15]

Such poor target attainment clearly warrants further investigation. DYSIS II was established to quantify the prevalence, characteristics, and treatment of hyperlipidemia in individuals with CHD or an acute coronary syndrome (ACS). Here, we present the data collected from these very high-risk patients in the UAE.

METHODS

Patients

Patients were recruited from two centers in the UAE from November 2013 to November 2014. Individuals were enrolled if they were diagnosed with either stable CHD or were hospitalized due to an ACS, were over 18 years of age, and had a full lipid profile available. ACS was defined as an ST-segment elevation myocardial infarction (STEMI)/left bundle branch block myocardial infarction (LBBB MI), non-ST-STEMI (NSTEMI), or unstable angina (UA). For patients with CHD, the last blood test before enrollment was evaluated to provide the lipid profile; for patients with an ACS, a blood test carried out within 24 h of admission to hospital was used. Patients were excluded if they were participating in a clinical trial at the same time as the study. ACS patients that died during hospitalization were also excluded. If any patients were receiving LLT, the duration of treatment had to be ≥3 months before enrollment. For the patients with stable CHD, data were collected at the baseline physician visit. For patients hospitalized owing to an ACS, data were collected on admission to hospital and at 4 months (±15 days) postadmission.

All patients that were enrolled provided written informed consent. The study received ethical approval from the relevant committees at each participating center and was carried out in accordance with the Declaration of Helsinki and its amendments.

Documentation

Data were first recorded on a standardized case report form (CRF) and were then entered into a central online database maintained at the Institut für Herzinfarktforschung, Ludwigshafen, Germany.

Patient demographics, cardiovascular risk factors, comorbidities, and current LLT were documented at enrollment. These included age, gender, and body mass index (BMI); current smoking or a sedentary lifestyle; presence of type 2 diabetes mellitus or hypertension; a history of CHD, chronic renal failure (CRF), chronic kidney disease, or peripheral artery disease; a prior MI or stroke (ischemic or hemorrhagic); and any family history of CHD. Obesity was defined as BMI >30 kg/m^2. 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 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/week. Cardiovascular medications used at admission were also documented, including ACE inhibitors, antiplatelet agents, beta-blockers, calcium channel blockers, and diuretics. A full lipid profile was recorded, which included serum levels of total cholesterol (TC), LDL-C, high-density lipoprotein cholesterol (HDL-C), non-HDL-C, and triglycerides.

For ACS patients, preadmission cardiovascular risk status was determined according to the ESC/EAS guidelines, with targets for LDL-C for very high risk, high risk, moderate risk, and low-risk patients defined as <70 mg/dl (1.8 mmol/l), <100 mg/dl (2.6 mmol/l), <115 mg/dl (3.0 mmol/l), and <130 mg/dl (3.4 mmol/l), respectively.[10] Very high and high-risk patients are determined according to the presence of comorbidity, while risk factors or markers such as obesity and high C-reactive protein are additionally taken into account for determining moderate and low cardiovascular risk. LDL-C goal attainment by risk status was based on the lipid values determined at admission, which reflected lipid levels from the preadmission period. The median distance to the LDL-C target was calculated for patients who had not attained this level at the time of the lipid profile.

Patients were divided into subgroups based on whether they were being treated with LLT at the time of the latest lipid test (CHD patients) or admission to hospital (ACS patients). The following classes of LLT were assessed: statin monotherapy, nonstatin monotherapy, statin plus ezetimibe, and statin plus other nonstatin therapy (other nonstatins included nicotinic acid, fibrates, omega-3 fatty acids, and other less common agents). The statins assessed were atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin. Atorvastatin-equivalent daily dosages were based on clinical trial data regarding the LDL-C-lowering efficacy of various statins.[16]

For ACS patients, at 4 months (±15 days) postadmission, any lipid profiles collected since hospital discharge were obtained, and the medications that the subjects were receiving at this time were documented. Any cardiovascular-related adverse events that occurred during the follow-up period were recorded. These were not mutually exclusive and included rehospitalization, MI, stroke, percutaneous coronary intervention, and coronary artery bypass grafting.

Statistics

Throughout the text, the term "LLT-treated" refers to the treatment status at the time of the lipid test, either that before the enrolment visit (CHD patients) or that at admission for the initial ACS. Data are presented as means with standard deviations, medians with interquartile ranges, or absolute values with percentages. LDL-C target attainment was assessed first by risk classification and then, in the subgroup of patients with LDL-C data at both admission and follow-up. The Chi-squared test or the Mann–Whitney–Wilcoxon test was used as appropriate to determine statistical significance for any comparisons. Data analysis was performed using SAS version 9.2 (Cary, NC, USA).

RESULTS

Patients

A total of 416 patients were recruited, 216 with stable CHD and 200 with an ACS. The mean age of the CHD individuals was 65.9 ± 11.2 years and 65.3% (141/216) were male [Table 1]. The majority of subjects were Arabic (92.1%; 199/216), with Indians making up 5.6% (12/216). Obesity (BMI >30 kg/m^2) was highly prevalent at 46.8% (101/216), while only 8.8% (19/216) of patients were noted to be current smokers. Comorbidities were common, in particular, type 2 diabetes mellitus (84.3%; 182/216) and hypertension (89.4%; 193/216). Only five of the 216 patients were not being treated with LLT at the time of enrollment.

The patients with an ACS had a mean age of 55.6 ± 10.8 years and 87.5% (175/200) were male [Table 2]. In terms of ethnicity, 49.5% (99/200) were Arab and 39.0% (78/200) were Indian. Obesity was documented for 23.5% (47/200), while 27.0% (54/200) were current smokers and 85% (170/200) reported a sedentary lifestyle. Of the 200 patients enrolled, 129 (64.5%) were being treated with LLT before their ACS. This group of subjects was slightly older than the no LLT group (57.3 vs. 52.5 years; $P = 0.0028$) and contained a lower proportion of smokers (21.7% vs. 36.6%; $P = 0.023$). All other characteristics were similar for the LLT and no LLT patients. Comorbidities were more common for the LLT group in comparison to the no LLT, in particular, type 2 diabetes (55.0% vs. 23.9%; $P = 0.00002$) and hypertension (72.1% vs. 39.4%; $P < 0.00001$). A smaller proportion of the LLT group was diagnosed with a STEMI or an MI/LBBB in comparison to the no LLT group (39.5% vs. 57.7%; $P = 0.013$). The rate of NSTEMI was similar between groups, while UA was more often diagnosed for the LLT group (20.2% vs. 8.5%; $P = 0.031$).

Lipid profile at the time of latest lipid test

The mean LDL-C level of the LLT-treated patients with stable CHD was slightly above the recommended target at 81.7 ± 32.7 mg/dl [Table 3]. The median HDL-C level was 41.0 (32.0, 49.0) mg/dl, the median non-HDL-C level was 100.0 (82.0, 127.0) mg/dl, the median TC level was 147.0 (121.0, 169.0) mg/dl, and the median triglyceride level was 122.0 (87.0, 168.0) mg/dl. A total of 39.3% (83/211) of the LLT-treated CHD patients had an LDL-C level of <70 mg/dl, with the median distance to this value being 23.0 (8.5, 44.0) mg/dl. Multivariate logistic regression identified type 2 diabetes mellitus as being predictive of achieving an LDL-C level below 70 mg/dl (odds ratio [OR]: 3.01; 95% confidence interval [CI]: 1.03–8.73; P 0.043), while patients aged 70 years or older were less likely to reach this target (OR: 0.34; 95% CI: 0.17–0.70; $P = 0.0032$) [Table 4].

For the LLT-treated ACS patients, the mean LDL-C level was 94.0 ± 38.6 mg/dl, LDLC-C < 70 mg/dl based on ESC/EAS guidelines [Table 3].[10] The median HDL-C level was 34.0 (29.0, 40.0) mg/dl, the median non-HDL-C level was 116.0 (91.0, 148.0) mg/dl, the median TC level was 155.0 (125.0, 186.0) mg/dl, and the median triglyceride level was 143.0 (94.0, 203.0) mg/dl. An LDL-C level of <70 mg/dl was attained by 33.3% (43/129) of the LLT-treated ACS patients, with the median distance to this target being 38.0 (22.0, 60.0) mg/dl. When subdivided according to preadmission risk status, 33.3% of the 93 very high-risk LLT-treated ACS patients had reached their LDL-C target of <70 mg/dl, 44.4% of the 9 high-risk patients had achieved their target of <100 mg/dl, 66.7% of the 15 moderate-risk patients had achieved their target of <115 mg/dl, and 90.9% of the 11 low-risk patients had achieved their target of <130 mg/dl [Figure 1]. Out of the variables investigated in the multivariable analysis, stable angina was found to be predictive of achieving an LDL-C level of <70 mg/dl [OR: 5.00; 95% CI: 1.30–19.21; P 0.020; Table 4].

During the 4-month follow-up, new lipid profiles were available for only 29 of the ACS patients, 19 of those being treated with LLT at baseline and 10 of those that were not. For this group of patients, target attainment rose from 32.1% (9/28) at baseline to 44.8% (13/29) at 4 months.

Lipid-lowering therapy at the time of latest lipid test

At enrollment, 97.7% (211/216) of the patients with stable CHD were being treated with LLT [Table 5]. The majority of patients were receiving a statin as part of their treatment, with atorvastatin being the most commonly prescribed (71.3%; 149/209). When normalized to atorvastatin potency,[16] the mean daily statin dosage was 29 ± 15 mg. About 13.7% (29/211) of the CHD patients were being treated with ezetimibe in addition to a statin, with 7.6% (16/211) taking a statin plus other nonstatin medication.

Of the 198 ACS patients with available information, 64.6% were receiving LLT before admission, with all of these taking a statin as part of their treatment regimen. Atorvastatin was the most commonly prescribed (60.9%; 78/128). Only a single patient was being treated with a statin plus ezetimibe, while two (1.6%) were being treated with a statin plus other nonstatin. The mean atorvastatin-equivalent daily statin dosage was 23 ± 13 mg.

At the 4-month follow-up point, it was found that 97.0% (161/166) of the ACS patients were being treated with LLT, with all but one of these taking a statin as part of their therapy [Table 5].[16] Atorvastatin was used in the majority of cases (83.1%; 133/160), with rosuvastatin being the next most common (15.0%; 24/160). The use of nonstatin agents was rare, with one patient (0.6%) taking a statin plus ezetimibe and six (3.7%) taking a statin plus other nonstatin.

Events during follow-up for acute coronary syndrome patients

No patients died during the 4-month follow-up period, but nine (4.9%) required rehospitalization. Of these, a single rehospitalization was necessary in seven cases, with three or more needed in the other two. An ACS was stated as the reason for the first readmission in only two cases.

DISCUSSION

Hyperlipidemia was found to be widespread in patients with stable CHD and those hospitalized for an ACS in the UAE. While LDL-C target achievement appeared to be higher than reported for other countries, it was still poor. LLT was extensively used, especially in patients with established CHD; however, statin dosages were not maximized. There is clearly wide scope for improvements in how LLT is prescribed in these very high-risk patients.

Patients

The patients with stable CHD had extreme levels of cardiovascular risk factors and comorbidities. Obesity was highly prevalent, being reported for almost half of the subjects. In a recent survey, obesity was found for 19.6% of the general population of the UAE,[4] while a cardiovascular screening program involving native Emiratis demonstrated a rate of 35.4%.[2] Such a high frequency of this risk factor in the general population would understandably translate to a higher prevalence in our CHD patients, which were predominantly Arabic. This worrying level of obesity has been linked to the rapid changes in lifestyle that have accompanied the oil-driven economic growth of the UAE.[1] The high-calorie diet and sedentary lifestyle now adopted by much of the population also helps to explain the alarming prevalence of diabetes mellitus (84.7%) that was found in the patients with stable CHD in our study. Again, the rate of diabetes reported for the general population provides some rationalization for this finding. In a survey carried out in the year 2000, 20.2% of included subjects had a diagnosis of diabetes, with the rate being 24.5% when considering only native UAE citizens.[3] More recent studies have reported values of just over 30%, indicating a growing problem.[4,17] In the first DYSIS study, 66.9% of the Middle Eastern statin-treated patients had diabetes,[18] while in CEPHEUS-Arabian Gulf, the value was 63.5%.[14] In terms of hypertension, almost 90% of our CHD patients displayed this, a value that is higher than the 78.1% found in DYSIS-Middle East and 66.6% in CEPHEUS-Arabian Gulf.[14,18] These high rates of risk factors demonstrate the extremely poor cardiovascular health of these predominantly Arab CHD patients.

The patients enrolled owing to hospitalization for an ACS were younger than those with stable CHD, and the racial makeup of the group differed significantly. While most of the CHD patients were Arabic, almost 40% of those with an ACS were of Indian origin. There were also large differences in terms of the prevalence of cardiovascular risk factors. The rate of obesity (23.5%) was closer to that described for the general population of the UAE (19.6%).[4] This may be explained by the differences between South Asian expatriates and native UAE citizens within this prior screening study, with obesity rates of 14.1% and 46.6%, respectively, being documented.[4] Similar findings were observed for the prevalence of diabetes mellitus in our study. While a significant proportion of the ACS patients had this condition, it was approximately 40% smaller than that of the CHD patients. Again, Yusufali *et al*. described a higher rate of diabetes in native UAE citizens in comparison to South Asian expatriates.[4] A sedentary lifestyle was common for the ACS patients, a problem linked to the urbanization of the UAE and increasing dependence on modern technology.[1] In combination, these studies show alarming levels of cardiovascular risk factors in the Arab population of the UAE.

Lipid profile and low-density lipoprotein cholesterol target attainment

Despite the poor cardiovascular health of the patients with stable CHD, the mean LDL-C level for the LLT group was only approximately 10 mg/dl above the recommended target of <70 mg/dl, with 39.3% having attained this goal. While such target achievement is poor, it is higher than that reported for the very high-risk patients in other studies. In the most recent EUROASPIRE report, only 19.5% of CHD patients had an LDL-C level at goal, despite widespread use of LLT,[19] while in the Middle East, CEPHEUS-Levant gave a value of 24.8%.[15] In the first DYSIS study, the UAE and Kuwait combined had the highest target attainment rate for very high-risk patients of all 30 countries included in the analysis (44.9%).[12] In comparison, 26.6% of the Middle East and Africa patients reached the target, 19.1% of those from Europe/Canada/Israel, and 23.9% of those from China.[13] The consistently superior LDL-C levels found in the UAE compared to other countries are surprising given the aforementioned rates of cardiovascular risk factors and comorbidities and require further investigation. However, the extremely high prevalence of type 2 diabetes mellitus is likely to play a significant role, with the presence of this condition being found to be predictive of target attainment. The lipid profile characteristic of type 2 diabetes includes an atherogenic combination of high levels of triglycerides and low levels of HDL-C, while elevated LDL-C is less common.[20,21] Therefore, although LDL-C target attainment appears superior in the UAE, alternative lipid abnormalities should not be overlooked.

Lipid abnormalities were more abundant for the ACS patients, with high LDL-C combined with low HDL-C levels. Accordingly, the proportion of LLT-treated patients that had attained the <70 mg/dl goal was lower at 33.3%. A further point to note is that very few of the ACS patients had a repeat lipid test performed during the 4-month follow-up. This suggests poor monitoring of such high-risk patients. Improved follow-up may reduce the occurrence of recurrent adverse cardiovascular events.

Lipid-lowering therapy

Almost all of the patients with stable CHD were being treated with LLT at the time of their latest lipid test; however, the high proportion of patients that were not at the LDL-C target suggests that the therapy was not being administered effectively. For the ACS patients, a lower proportion was being treated with LLT before admission, but this increased significantly after hospitalization. The atorvastatin-equivalent dosage was low before the ACS admission, and although it increased up to follow-up, it remained below 40 mg/day. Guidelines recommend initiating intensive statin therapy after an ACS,[10] the benefits of which have been shown in numerous trials. Nicholls *et al*. demonstrated significant coronary plaque regression with intensive statin therapy in comparison to a standard.[22] In the Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in MI 22 study, patients were found to have a lower likelihood of death or a major cardiovascular event after suffering an ACS if treated with intensive rather than standard therapy.[23,24] In the IDEAL study, no difference in the rates of major coronary events was seen, but intensive therapy led to improvements in the achievement of other cardiovascular endpoints such as nonfatal MI.[25] In these and other studies, an atorvastatin dosage of 80 mg was generally used as the intensive arm,[26,27] a value that is much higher than the average of 39 mg found in the present analysis. This highlights the significant under-use of LLT in these very high-risk patients. The inadequate use of statins may have been influenced by the known dose-dependent side-effects causing reluctance on the part of the physician to prescribe high doses.[28,29]

The addition of a nonstatin agent such as ezetimibe or a fibrate is an alternative means by which LLT can be intensified, in particular for patients who cannot tolerate high doses of statins. In the Vytorin Efficacy International Trial, it was shown that, in patients that had suffered an ACS, LDL-C levels were lowered more effectively when ezetimibe was added to simvastatin treatment (93.8–53.7 mg/dl during the trial) than when simvastatin was used alone (93.8–69.5 mg/dl during the trial).[30] A 2% lower rate of primary endpoint achievement (cardiovascular death, nonfatal MI, UA requiring hospitalization, coronary revascularization, or nonfatal stroke) was also demonstrated for the patients receiving combination therapy. Increased plaque regression in patients with CHD has also been demonstrated for ezetimibe used with rosuvastatin in comparison to rosuvastatin used alone.[31,32] In the present study, the use of nonstatin LLT was quite common for the patients with CHD, with over 20% using combination therapy. For the ACS patients, however, use of such treatment was limited to just a few cases both at admission and at follow-up. This perhaps indicates a missed opportunity for intensification of LLT after an ACS.

The small number of events and rehospitalizations that occurred during the follow-up period prevents us from making comparisons between treatment patterns and cardiovascular outcome. Therefore, the true effect of this under-treatment cannot be demonstrated.

Limitations

One limitation of this analysis is that the relatively small size of the population resulted in very few patients with stable CHD that were not being treated with LLT at enrollment, making the statistical value of any comparisons low. The small number of patients with a new lipid profile available at follow-up was a further drawback, again preventing useful comparisons being made. However, this demonstrates poor monitoring of ACS patients after hospital discharge, which is a finding in itself. A further limitation was that only two centers were included. The short follow-up time resulted in few adverse events being recorded, preventing the identification of any associations between lipid levels, treatment strategies, and cardiovascular outcome.

CONCLUSIONS

Although the rate of attainment of the recommended LDL-C target of <70 mg/dl was higher in the UAE than those reported for other countries, it was still poor. LLT was widely used in both patients with stable CHD and those with an ACS; however, treatment was rarely maximized. As shown in this and other studies, in native Emiratis, in particular, rates of comorbidities are alarmingly high in the UAE. In order to reduce morbidity and mortality in this country, more effective treatment strategies for hyperlipidemia and associated cardiovascular risk factors need to be rapidly employed.

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Conflicts of interest

Wael Al Mahmeed (WAM) received Honoraria from Merck & Co., Inc., Kenilworth, NJ, USA for contributions to the DYSIS Study. Sherif Bakir (SB) did not receive consultancy fees as per internal agreement with the lead author. Salem Beshyah (SAB) received consultancy fees or research funds from Merck & Co., Inc., Kenilworth, NJ, USA. Anselm Gitt (AKG) received honoraria from Merck & Co., Inc., Kenilworth, NJ, USA for contributions to the DYSIS study. Martin Horack (MH) reports that his institution received funding for recruitment and biostatistics for the DYSIS registry. At the time of the study, Ami Vyas (AV) was a full-time employee of Rutgers University, which received grant funding for this project from Merck & Co., Inc., Kenilworth, NJ, USA. AV is currently employed by the University of Rhode Island. Bassem Morcos (BM), Sameh Wajih (SW), Dominik Lautsch (DL), Philippe Brudi (PBru), Carl Baxter (CAB) and Baishali Ambegaonkar (BA) are employees of the sponsor.

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REFERENCES

1. Loney T, Aw TC, Handysides DG, Ali R, Blair I, Grivna M, et al. An analysis of the health status of the United Arab Emirates: The 'big 4' public health issues. Glob Health Action. 2013;6:20100. [PMCID: PMC3566378] [PubMed: 23394856]

2. Hajat C, Harrison O, Al Siksek Z. Weqaya: A population-wide cardiovascular screening program in abu Dhabi, United Arab Emirates. Am J Public Health. 2012;102:909–14. [PMCID: PMC3483896] [PubMed: 21940918]

3. Malik M, Bakir A, Saab BA, King H. Glucose intolerance and associated factors in the multi-ethnic population of the United Arab Emirates: Results of a national survey. Diabetes Res Clin Pract. 2005;69:188–95. [PubMed: 16005369]

4. Yusufali A, Bazargani N, Muhammed K, Gabroun A, AlMazrooei A, Agrawal A, et al. Opportunistic screening for CVD risk factors: The Dubai Shopping for Cardiovascular Risk Study (DISCOVERY) Glob Heart. 2015;10:265–72. [PubMed: 26271552]

5. Aw TC. Global public health and the United Arab Emirates. Asia Pac J Public Health. 2010;22:19S–24S. [PubMed: 20566529]

6. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: Prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet. 2005;366:1267–78. [PubMed: 16214597]

7. Ewang-Emukowhate M, Wierzbicki AS. Lipid-lowering agents. J Cardiovasc Pharmacol Ther. 2013;18:401–11. [PubMed: 23811423]

8. Cholesterol Treatment Trialists' (CTT) Collaboration. Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L, et al. Efficacy and safety of LDL-lowering therapy among men and women: Meta-analysis of individual data from 174,000 participants in 27 randomised trials. Lancet. 2015;385:1397–405. [PubMed: 25579834]

9. Anderson TJ, Grégoire J, Hegele RA, Couture P, Mancini GB, McPherson R, et al. 2012 update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol. 2013;29:151–67. [PubMed: 23351925]

10. European Association for Cardiovascular Prevention & Rehabilitation. Reiner Z, Catapano AL, De Backer G, Graham I, Taskinen MR, et al. ESC/EAS guidelines for the management of dyslipidaemias: The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) Eur Heart J. 2011;32:1769–818. [PubMed: 21712404]

11. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol. 2014;63:2889–934. [PubMed: 24239923]

12. Gitt AK, Lautsch D, Ferrieres J, Kastelein J, Drexel H, Horack M, et al. Contemporary data on low-density lipoprotein cholesterol target value attainment and distance to target in a cohort of 57,885 statin-treated patients by country and region across the world. Data Brief. 2016;9:616–20. [PMCID: PMC5066206] [PubMed: 27766290]

13. Gitt AK, Lautsch D, Ferrieres J, Kastelein J, Drexel H, Horack M, et al. Low-density lipoprotein cholesterol in a global cohort of 57,885 statin-treated patients. Atherosclerosis. 2016;255:200–9. [PubMed: 27667299]

14. Arafah M, Al-Hinai AT, Al Mahmeed W, Al-Rasadi K, Al Tamimi O, Al Herz S, et al. Centralized pan-middle east survey on the undertreatment of hypercholesterolemia: Results from the CEPHEUS study in Arabian Gulf countries. Angiology. 2014;65:919–26. [PubMed: 24301426]

15. Hammoudeh AJ, Echtay A, Ghanem GY, Haddad J CEPHEUS-Levant survey investigators. Achieving low-density lipoprotein cholesterol treatment goals among dyslipidemic individuals in the levant: The CEntralized pan-levant survey on tHE undertreatment of hypercholeSterolemia (CEPHEUS) study. Curr Med Res Opin. 2014;30:1957–65. [PubMed: 24889279]

16. Roberts WC. The rule of 5 and the rule of 7 in lipid-lowering by statin drugs. Am J Cardiol. 1997;80:106–7. [PubMed: 9205036]

17. Alsheikh-Ali AA, Omar MI, Raal FJ, Rashed W, Hamoui O, Kane A, et al. Cardiovascular risk factor burden in Africa and the Middle East: The Africa Middle East cardiovascular epidemiological (ACE) study. PLoS One. 2014;9:e102830. [PMCID: PMC4121128] [PubMed: 25090638]

18. Al Sifri SN, Almahmeed W, Azar S, Okkeh O, Bramlage P, Jünger C, et al. Results of the dyslipidemia international study (DYSIS)-middle east: Clinical perspective on the prevalence and characteristics of lipid abnormalities in the setting of chronic statin treatment. PLoS One. 2014;9:e84350. [PMCID: PMC3882235] [PubMed: 24400085]

19. Kotseva K, Wood D, De Bacquer D, De Backer G, Rydén L, Jennings C, et al. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. Eur J Prev Cardiol. 2016;23:636–48. [PubMed: 25687109]

20. Krauss RM. Lipids and lipoproteins in patients with type 2 diabetes. Diabetes Care. 2004;27:1496–504. [PubMed: 15161808]

21. Taskinen MR, Borén J. New insights into the pathophysiology of dyslipidemia in type 2 diabetes. Atherosclerosis. 2015;239:483–95. [PubMed: 25706066]

22. Nicholls SJ, Ballantyne CM, Barter PJ, Chapman MJ, Erbel RM, Libby P, et al. Effect of two intensive statin regimens on progression of coronary disease. N Engl J Med. 2011;365:2078–87. [PubMed: 22085316]

23. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004;350:1495–504. [PubMed: 15007110]

24. Ray KK, Cannon CP, McCabe CH, Cairns R, Tonkin AM, Sacks FM, et al. Early and late benefits of high-dose atorvastatin in patients with acute coronary syndromes: Results from the PROVE IT-TIMI 22 trial. J Am Coll Cardiol. 2005;46:1405–10. [PubMed: 16226162]

25. Pedersen TR, Faergeman O, Kastelein JJ, Olsson AG, Tikkanen MJ, Holme I, et al. High-dose atorvastatin vs.usual-dose simvastatin for secondary prevention after myocardial infarction: The IDEAL study: A randomized controlled trial. JAMA. 2005;294:2437–45. [PubMed: 16287954]

26. Cannon CP, Steinberg BA, Murphy SA, Mega JL, Braunwald E. Meta-analysis of cardiovascular outcomes trials comparing intensive versus moderate statin therapy. J Am Coll Cardiol. 2006;48:438–45. [PubMed: 16875966]

27. Josan K, Majumdar SR, McAlister FA. The efficacy and safety of intensive statin therapy: A meta-analysis of randomized trials. CMAJ. 2008;178:576–84. [PMCID: PMC2244680] [PubMed: 18299547]

28. Hirsh BJ, Smilowitz NR, Rosenson RS, Fuster V, Sperling LS. Utilization of and adherence to guideline-recommended lipid-lowering therapy after acute coronary syndrome: Opportunities for improvement. J Am Coll Cardiol. 2015;66:184–92. [PubMed: 26160634]

29. Morrissey RP, Diamond GA, Kaul S. Statins in acute coronary syndromes: Do the guideline recommendations match the evidence? J Am Coll Cardiol. 2009;54:1425–33. [PubMed: 19796735]

30. Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med. 2015;372:2387–97. [PubMed: 26039521]

31. Wang X, Zhao X, Li L, Yao H, Jiang Y, Zhang J, et al. Effects of combination of ezetimibe and rosuvastatin on coronary artery plaque in patients with coronary heart disease. Heart Lung Circ. 2016;25:459–65. [PubMed: 26687339]

32. Masuda J, Tanigawa T, Yamada T, Nishimura Y, Sasou T, Nakata T, et al. Effect of combination therapy of ezetimibe and rosuvastatin on regression of coronary atherosclerosis in patients with coronary artery disease. Int Heart J. 2015;56:278–85. [PubMed: 25902885]

Figures and Tables

Table 1

Patient characteristics - stable coronary heart disease cohort

	Total (n=216)	LLT (n=211)	No LLT (n=5)
Age (years)	65.9±11.2	65.7±11.1	74.2±15.8
Male (%)	65.3 (141/216)	64.5 (136/211)	100.0 (5/5)
Race/ethnicity			
Arabic	92.1 (199/216)	91.9 (194/211)	100.0 (5/5)
Indian	5.6 (12/216)	5.7 (12/211)	0.0 (0/5)
Black	0.9 (2/216)	0.9 (2/211)	0.0 (0/5)
Caucasian	0.5 (1/216)	0.5 (1/211)	0.0 (0/5)
Filipino	0.5 (1/216)	0.5 (1/211)	0.0 (0/5)
Unknown	0.5 (1/216)	0.5 (1/211)	0.0 (0/5)
BMI (kg/m^2)	29.6 (25.7-33.7)	29.6 (25.7-33.8)	28.3 (26.0-30.9)
BMI >30 kg/m^2 (%)	46.8 (101/216)	46.9 (99/211)	40.0 (2/5)
SBP (mmHg)	130 (117-145)	130 (116-145)	124 (122-140)
DBP (mmHg)	68 (60-75)	68 (60-75)	74 (62-76)
CV risk factors (%)			
Current smoker	8.8 (19/216)	8.5 (18/211)	20.0 (1/5)
Sedentary lifestyle	83.9 (178/212)	84.1 (175/208)	75.0 (3/4)
Family history of CHD	25.2 (35/139)	25.9 (35/135)	0.0 (0/4)
Comorbidities (%)			
Type 2 diabetes mellitus	84.3 (182/216)	84.8 (179/211)	60.0 (3/5)
Hypertension	89.4 (193/216)	89.6 (189/211)	80.0 (4/5)

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*Includes ischemic and hemorrhagic stroke, #>3 months prior to enrollment. LLT: Lipid-lowering therapy, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CV: Cardiovascular, CHD: Coronary heart disease, CKD: Chronic kidney disease, PAD: Peripheral artery disease, ACS: Acute coronary syndrome, SD: Standard deviation, CABG: Coronary artery bypass grafting, IQR: Interquartile range, PCI: Percutaneous coronary intervention. Data presented as median (IQR), mean±SD, or percentage (n/N). P values not calculated due to small sample size

Table 2

Patient characteristics - acute coronary syndrome cohort

	Total (n=200)	LLT (n=129)	No LLT (n=71)	P (LLT vs. no LLT)
Age (years)	55.6±10.8	57.3±9.8	52.5±12.0	0.0028
Male (%)	87.5 (175/200)	85.3 (110/129)	91.5 (65/71)	0.20
Race/ethnicity				
Arabic	49.5 (99/200)	49.6 (64/129)	49.3 (35/71)	0.97
Indian	39.0 (78/200)	40.3 (52/129)	36.6 (26/71)	0.61
Black	0.5 (1/200)	0.8 (1/129)	0.0 (0/71)	0.46
Caucasian	1.5 (3/200)	0.8 (1/129)	2.8 (2/71)	0.26
Filipino	3.0 (6/200)	4.7 (6/129)	0.0 (0/71)	0.07
Other Asian	6.5 (13/200)	3.9 (5/129)	11.3 (8/71)	<0.05
BMI (kg/m^2)	27.2 (24.4-29.8)	27.5 (24.3-30.1)	27.0 (24.5-29.0)	0.35
BMI >30 kg/m^2 (%)	23.5 (47/200)	27.1 (35/129)	16.9 (12/71)	0.10
SBP (mmHg)	123 (110-141)	120 (110-140)	124 (114-141)	0.25
DBP (mmHg)	73 (63-82)	73 (62-81)	71 (65-84)	0.50
CV risk factors (%)				
Current cigarette smoker	27.0 (54/200)	21.7 (28/129)	36.6 (26/71)	0.023
Sedentary lifestyle	85.0 (170/200)	86.8 (112/129)	81.7 (58/71)	0.33
Family history of CHD	22.3 (43/193)	28.7 (35/122)	11.3 (8/71)	<0.01
Comorbidities (%)				
Type 2 diabetes mellitus	44.0 (88/200)	55.0 (71/129)	23.9 (17/71)	0.00002
Hypertension	60.5 (121/200)	72.1 (93/129)	39.4 (28/71)	<0.00001

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*Includes ischemic and hemorrhagic stroke. LLT: Lipid-lowering therapy, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CV: Cardiovascular, CHD: Coronary heart disease, CKD: Chronic kidney disease, PAD: Peripheral artery disease, ACS: Acute coronary syndrome, STEMI: ST-segment elevation myocardial infarction, LBBB MI: Myocardial infarction with left bundle branch block, NSTEMI: Non-ST-elevation myocardial infarction, SD: Standard deviation, IQR: Interquartile range. Data presented as median (IQR), mean±SD, or percentage (n/N). P values calculated using Chi-squared test or Mann–Whitney–Wilcoxon test

Table 3

Lipid profile (latest blood test*)

	Stable CHD			ACS			
	Total (n=216)	LLT (n=211)	No LL (n=5)	Total (n=200)	LLT (n=129)	No LLT (n=71)	P (LLT vs. no LLT)
LDL-C (mg/dl), mean±SD	82.5±32.9	81.7±32.7	118.2±19.4	105.0±44.9	94.0±38.6	124.9±49.0	<0.0001
HDL-C (mg/dl), median (IQR)	41.0 (33.0-49.0)	41.0 (32.0-49.0)	44.0 (36.0-46.0)	35.0 (29.0-41.0)	34.0 (29.0-40.0)	35.0 (30.0-45.0)	
Non-HDL-C (mg/dl), median (IQR)	101.5 (83.0-127.0)	100.0 (82.0-127.0)	147.0 (126.0-173.0)	136.0 (104.0-168.5)	116.0 (91.0-148.0)	153.0 (125.0-190.0)	
TC (mg/dl), mean±SD	148.9±36.4	147.8±35.8	196.0±30.0	175.6±54.3	161.6±46.7	201.0±58.0	<0.0001
Triglycerides (mg/dl), median (IQR)	122.5 (88.5-166.5)	122.0 (87.0-168.0)	148.0 (114.0-160.0)	142.5 (97.0-198.0)	143.0 (94.0-203.0)	142.0 (105.0-195.0)	
LDL-C <70 mg/dl#	38.4 (83/216)	39.3 (83/211)	0.0 (0/5)	23.6 (47/199)	33.3 (43/129)	5.7 (4/70)	<0.0001
Distance to LDL-C <70 mg/dl	24.0 (9.0-45.0)	23.0 (8.5-44.0)	44.0 (38.0-62.0)	42.0 (24.0-71.5)	38.0 (22.0-60.0)	54.5 (32.0-78.0)	<0.01

*CHD patients: Last recorded lipid profile prior to physician visit, ACS patients: Within 24 h of admission for ACS event, #ESC/EAS guidelines. LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TC: Total cholesterol, LLT: Lipid-lowering therapy, CHD: Coronary heart disease, ACS: Acute coronary syndrome, SD: Standard deviation, IQR: Interquartile range, ESC: European Society of Cardiology, EAS: European Atherosclerosis Society. Data presented as median (IQR) or percentage (n/N). P values for LLT versus no LLT in the ACS cohort calculated using Chi-squared test or Mann–Whitney–Wilcoxon test. P values not calculated for LLT versus no LLT in the stable CHD cohort due to small sample size

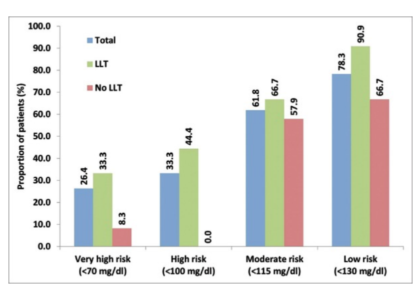
Table 4

Multiple logistic regression model for low-density lipoprotein cholesterol< 70 mg/dl for patients receiving lipid-lowering therapy at baseline

Variable	CHD patients		ACS patients	
	OR (95% CI)	P	OR (95% CI)	P
Age ≥70 years	0.34 (0.17-0.70)	0.0032	0.67 (0.12-3.74)	0.64
Female gender	0.54 (0.27-1.11)	0.09	0.82 (0.23-2.92)	0.76
BMI >30 kg/m^2	0.84 (0.43-1.63)	0.61	1.34 (0.54-3.61)	0.50
Current smoking*	0.60 (0.18-2.00)	0.40	-	-
Sedentary lifestyle	0.67 (0.29-1.56)	0.35	4.63 (0.72-29.78)	0.11
Stable angina	0.44 (0.22-0.89)	0.02	5.00 (1.30-19.21)	0.020
Type 2 diabetes	3.01 (1.03-8.73)	0.043	1.78 (0.73-4.34)	0.20
Hypertension	0.53 (0.19-1.52)	0.24	0.43 (0.16-1.13)	0.087
Statin dose (calculated as atorvastatin equivalent, mg/day)	1.01 (0.99-1.03)	0.28	1.01 (0.98-1.05)	0.56
CKD	1.71 (0.85-3.45)	0.13	3.12 (0.57-17.07)	0.19
History of congestive heart failure	0.86 (0.41-1.83)	0.70	1.21 (0.25-5.95)	0.82

*ACS analysis excluded due to low number of patients. BMI: Body mass index, The model includes all displayed variables, which were selected based on clinical relevance. CHD: Coronary heart disease, ACS: Acute coronary syndrome, CI: Confidence interval, OR: Odds ratio, CKD: Chronic kidney disease

Figure 1



Target low-density lipoprotein cholesterol attainment in ACS patients (% at goal) by risk level prior to ACS Original figure. Risk level determined according the European Society of Cardiology/European Atherosclerosis Society guidelines. Total population: Very high risk: n = 129 (LLT 93, no LLT 36); high risk: n = 12 (LLT 9, no LLT 3); moderate risk: n = 34 (LLT 15, no LLT 19); low risk: n = 23 (LLT 11, no LLT 12)

Table 5

Lipid-lowering therapy at time of latest lipid test

	Stable CHD* (n=216)	ACS	
		Hospital admission (n=198)	4-month follow-up (n=166)
Treated with LLT (%)	97.7 (211/216)	64.6 (128/198)	97.0 (161/166)
Statin therapy (%)	96.8 (209/216)	64.6 (128/198)	96.4 (160/166)
Atorvastatin	71.3 (149/209)	60.9 (78/128)	83.1 (133/160)
Fluvastatin	0.0 (0/209)	0.0 (0/128)	0.0 (0/160)
Lovastatin	0.0 (0/209)	0.0 (0/160)	0.0 (0/160)
Pitavastatin	0.0 (0/209)	0.0 (0/128)	0.0 (0/160)
Pravastatin	1.9 (4/209)	0.0 (0/128)	0.6 (1/160)
Rosuvastatin	22.5 (47/209)	21.1 (27/128)	15.0 (24/160)
Simvastatin	3.8 (8/209)	3.9 (5/128)	0.6 (1/160)
Unknown	0.5 (1/209)	14.1 (18/128)	0.6 (1/160)
Statin daily dose - atorvastatin equivalents (mg/day)#	29±15 (n=208)	23±13 (n=110)	39±12 (n=159)
Statin daily dose - simvastatin equivalents (mg/day)#	58±31 (n=208)	47±25 (n=110)	79±25 (n=159)
Stain monotherapy (%)	77.7 (164/211)	97.7 (125/128)	95.0 (153/161)
Nonstatin monotherapy (%)	0.9 (2/211)	0.0 (0/128)	0.6 (1/161)
Statin + ezetimibe (%)	13.7 (29/211)	0.8 (1/128)	0.6 (1/161)
Statin + other nonstatin (%)	7.6 (16/211)	1.6 (2/128)	3.7 (6/161)

*LLT at time of latest lipid test, #Dose equivalents calculated according to reference.[16] Data presented as mean±SD, or percentage (n/N). P values calculated using Chi-squared test or Mann–Whitney–Wilcoxon test. SD: Standard deviation, LLT: Lipid-lowering therapy, CHD: Coronary heart disease, ACS: Acute coronary syndrome

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