Defining the prevalence of low HDL-C in a European cohort of dyslipidaemic patients

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Low HDL-cholesterol is increasingly recognized as an independent risk factor for adverse cardiovascular outcomes, irrespective of levels of LDL-cholesterol. Although sporadic reports suggest that the prevalence of low HDL-cholesterol is substantial, we lack detailed data on the true prevalence of this condition among patients receiving treatment for dyslipidaemia. The Pan-European survey on HDL-cholesterol has collected data on levels of HDL-cholesterol, together with other lipid parameters and cardiovascular risk factors, from more than 9000 dyslipidaemic patients by 1350 specialist physicians in 11 European countries. A preliminary analysis of a subset of the participants in the survey suggests a population at markedly elevated cardiovascular risk. The detailed information from this survey, currently under analysis, will define the magnitude of the contribution of low HDL-cholesterol to dyslipidaemia in Europe and will focus on the need to include strategies for correcting low HDL-cholesterol within multiple risk factor intervention programmes.

KEYWORDS
HDL-cholesterol; Prevalence; Atherosclerosis; Cardiovascular risk; Dyslipidaemia

Introduction

Epidemiological surveys and analyses of baseline characteristics of trial populations suggest a high prevalence of low HDL-cholesterol. For example, estimates of the proportions of men with HDL-cholesterol below cut-off points (usually 0.9 mmol/L (35 mg/dL) or 1.0 mmol/L (40 mg/dL)) range from 7 to 9% in France,1,2 15% in Mexico,3 15–23% in Holland (depending on age),5 17% in the UK,6 18% in the Rio de Janeiro area of Brazil,7 24% in India,30% in Canada,8 32% in Iran,9 7–38% in USA,10–14 and an astounding 75% in Thailand.15 Within these overall figures lie variations in the prevalence of low HDL-cholesterol due to ethnicity,16,17 a sharply increased prevalence in patients who have coronary artery disease,6,9,18 and different study designs.

These data are sufficient to strongly suggest that low HDL-cholesterol is a clinically significant problem in many areas. However, experience from the large cohort followed up in the PROspective Cardiovascular Münster (PROCAM) Study in Germany illustrates the importance of accurately defining regional differences in risk factor profiles, as these can impact strongly on the design of interventions and, ultimately, the prognosis of patients.19

No data on the epidemiology of low HDL-cholesterol are available from large-scale surveys in Europe and standardized, well-designed observational studies of sufficient size and geographical coverage are needed before we can estimate with confidence the magnitude of the therapeutic challenge posed by low HDL-cholesterol in Europe.

Accordingly, a major survey of levels of HDL-cholesterol in patients receiving treatment for dyslipidaemia has been carried out in a number of European countries. Detailed information on the management of cardiovascular risk, in general, in these patients was also sought in the survey. The survey results are under analysis, and this report focuses on the rationale and design of this study.
Design of the survey

Objectives

The primary objective of this survey was to determine the proportion of individuals with low HDL-cholesterol in a European population of dyslipidaemic patients. Low HDL-cholesterol was defined as a level of <1.0 mmol/L (<40 mg/dL) in men and <1.2 mmol/L (<50 mg/dL) in women. The characterization of co-existing risk factors by multivariate analysis was a secondary objective.

Inclusion criteria

Subjects were ambulatory males or females aged at least 18. Eligible subjects had also received at least 3 months prior treatment for hypercholesterolaemia and/or hypertriglyceridaemia by diet and exercise in combination with one or more lipid-lowering drugs, or had serum cholesterol ≥200 mg/dL (≥5.3 mmol/L) and/or serum triglycerides ≥180 mg/dL (≥2.0 mmol/L) despite at least 3 months treatment with diet and exercise, or had a secondary dyslipidaemia due to diabetes mellitus or associated with metabolic syndrome. Patients with primary dyslipidaemia, dyslipidaemia (hypercholesterolaemia and/or hypertriglyceridaemia) secondary to other causes than diabetes mellitus, or the metabolic syndrome (e.g. arising from the use of oral contraceptives, corticosteroids, or HIV-protease inhibitors) were not eligible.

Data acquisition

Power calculations, based on published estimates of the prevalence of low HDL-cholesterol, required the recruitment of 7000 subjects to provide a prevalence estimate with a two-sided 95% CI of 2%. Anticipating a lack of HDL-cholesterol values in 30% of the subjects, it was calculated that 9100 subjects should be enrolled.

Subjects were recruited by specialist physicians, who were mainly cardiologists or endocrinologists, and all were experienced in the management of dyslipidaemia. Each specialist contributed data from at least four subjects to the survey (each subject was the first, matching the enrolment criteria seen by the specialist on a given day). Data were gathered using a questionnaire (Table 1). Questionnaires could be returned via courier or the internet. Physicians were provided with information within the questionnaire on how to accurately measure the waist circumference (defined as the smallest horizontal circumference at waist level). No information that could identify a subject, directly or indirectly, was requested in the questionnaire, in line with European data protection requirements.

Several quality assurance measures were put in place. Participating physicians received several follow-up calls to explain the process and the questionnaire, and to address any questions. In addition, the questionnaire materials contained a checklist to ensure proper completion. It was a requirement of the survey that all biochemical/clinical chemistry data should have been obtained from the same blood sample or from blood samples taken on the same date and at the same time.

Results

At the end of the survey, data on 9317 patients had been acquired from 1350 physicians in 11 European countries (Figure 1). The detailed data will be published separately in 2005. However, a provisional analysis of approximately two-thirds of the study population suggests an elderly population (mean age >60 years), with a majority of males (about two-thirds). This was in general a high-risk population, judging from the spectrum of demographic parameters and cardiovascular risk factors. About one-sixth of this sample of the overall population were current smokers, about one-quarter had a history of myocardial infarction, about half were diabetic, and about two-thirds were sedentary (more than two sessions of physical exercise/week).

More than 80% were receiving treatment with lifestyle intervention and lipid-modifying drugs. Importantly, almost half of this provisional population met the National Cholesterol Education Panel/Adult Treatment Panel III definition of the metabolic syndrome.20

Discussion

We require more information on the true prevalence of low HDL-cholesterol in patients requiring treatment for
dyslipidaemia and to know whether therapies to correct low HDL-cholesterol are applied in an optimal way. HypoHDLaemia is indeed frequently unrecognized in hyperlipidaemic patients, despite the well-established role of HDL-cholesterol as an independent risk factor for cardiovascular disease. A recent study conducted in France indicates the magnitude of the problem: HDL-cholesterol was not measured in up to one-third of the hyperlipidaemic patients on statin treatment. Therefore, we are eager to have the final analyses of this Pan-European Survey on low HDL-cholesterol, still ongoing, which has gathered data from a substantial population who were, on average, at elevated risk of a cardiovascular event.

These data will be compared with landmark epidemiological analyses, including the Framingham study in the USA and the PROspective CArdiovascular Münster (PROCAM) study in Europe, which have confirmed the importance of low HDL-cholesterol in driving the progression of atherosclerosis and coronary disease.

Consistent with these aforementioned published observations, intervention with regimens including a HDL-cholesterol raiser, nicotinic acid being the most potent one available, has been associated with clinically and statistically significant improvements in clinical outcomes. Accordingly, interventions to correct low HDL-cholesterol, in addition to reducing LDL-cholesterol, will become increasingly important in the management of dyslipidaemia in the future.

It is our opinion that the data from this large-scale European survey will not only help in the design of treatment strategies for the management of dyslipidaemia today, but will also contribute importantly to tomorrow’s management algorithms for the control of cardiovascular risk. For example, current guidelines for the management of dyslipidaemia identify low HDL-cholesterol as a marker of risk and are yet to recognize this condition as a risk factor in its own right. Expert groups, including the European Consensus Panel on HDL-cholesterol among others, have called for greater emphasis on the management of low HDL-cholesterol in management guidelines for dyslipidaemia. Accurately defining the incidence of low HDL-cholesterol will help to focus attention on this important risk factor and will support the recognition of the importance of correcting low HDL-cholesterol in optimizing prognosis in patients at elevated risk of a cardiovascular event.

Conclusions

The Pan-European Survey on HDL-cholesterol has gathered data on the prevalence of low HDL-cholesterol and on other aspects of cardiovascular care, from a population of more than 9000 dyslipidaemic patients in 11 European countries. These data, currently undergoing detailed analysis, will help to define the scale of the problem of low HDL-cholesterol in routine cardiovascular care and will contribute to the design of optimized management strategies for reducing cardiovascular risk in the future.