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Non-achievement of LDL-cholesterol targets in patients with diabetes at very-high cardiovascular risk receiving statin treatment: Incidence and risk factors

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ABSTRACT

Background: Cardiovascular diseases are the first cause of mortality in patients with diabetes, and LDL-cholesterol is a well-established cardiovascular risk factor. This study aimed to assess rate of LDL-cholesterol target attainment among patients with diabetes at very-high cardiovascular risk treated with statins, and to identify predictive factors of non-attainment of target in this population.
Methods: Patients were recruited in the Nutrition-Diabetes unit of Montpellier University Hospital, France, from 2014 to 2017. We included all consecutive patients with type 1 or type 2 diabetes receiving statin treatment and at very-high cardiovascular risk according to 2016 ESC guidelines, therefore having a LDL-cholesterol target of <1.8 mmol/L. LDL-cholesterol levels were measured upon admission. Variables independently associated with non-attainment of LDL-Cholesterol target were assessed using multivariable logistic regression.
Results: 654 patients were included. Mean age was 63.8 years (SD 11.0), 41.9% were women and 42.3% had a history of cardiovascular disease. 59% of patients did not achieve LDL-cholesterol target, with a median value (interquartile range) of 2.4 mmol/L (2.1–2.9) versus 1.4 mmol/L (1.1–1.6) in patients at target. Risk of non-attainment of LDL-cholesterol target value was increased in women (odds ratio [95% confidence interval]: 2.27 [1.62–3.17]) and decreased in patients with history of coronary artery disease (0.64 [0.45–0.89]) or history of stroke or transient ischemic attack (0.59 [0.33–1.07]).
Conclusions: Management of dyslipidemia is suboptimal, even in very-high risk patients with diabetes under statins. Lipid-lowering treatment should be intensified, in particular in very high risk patients with diabetes who are women or in primary cardiovascular prevention.
Clinical Trial number: NCT03449784

1. Introduction

Cardiovascular diseases (CVD) are the leading cause of death in Europe, responsible for 45% of all deaths [1], and adults with diabetes mellitus (DM) are two to four times more likely to die from heart diseases than those without DM [2]. LDL-cholesterol (LDL-C) is one of the major risk factors for CVD, through its role in the development of atherosclerosis. The efficacy of statins has been demonstrated by a considerable amount of literature not only in lowering LDL cholesterol levels [3] but also in reducing cardiovascular (CV) events, both in DM and non-DM patients [4]. Their efficacy is favored by more-intensive treatment [5]. A meta-analysis of 14 randomized trials, evaluating the efficacy of cholesterol-lowering therapy in 18,686 people with DM, showed that for each 1.0 mmol/L reduction in LDL-C obtained with statins, risk of major vascular events significantly decreased by 21%, risk of coronary events by 22% and risk of vascular mortality by 13% [6]. Guidelines for the management of dyslipidemia have emerged from different countries [7–10]. If CV risk classification slightly differs

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between guidelines, all of them – including the latest French recommendations – defined a target of LDL-C < 1.8 mmol/L for very high risk patients. However, studies revealed an important gap between LDL-C target and LDL-C levels measured in different populations, particularly in very high risk patients. The DYSIS II study carried out in 18 countries showed that target value was reached by only 29.4% of patients with stable coronary heart disease and 18.9% of patients suffering from an acute coronary syndrome [11]. DYSIS II study showed that patients with type 2 DM were more likely to achieve targets than others [11]. However, LDL-C goal attainment has rarely been assessed specifically in DM population, in which CVD is of particular importance. This study aimed to assess the rate of LDL-C target value attainment (<1.8 mmol/L) among patients at very-high CV risk with DM, and to identify predictive factors of non-attainment of target in this population.

2. Material and methods

2.1. Study design, setting and participants

This observational study was carried out over a 3-year period from May 2014 to May 2017 in the Diabetes-Nutrition unit of the University Hospital of Montpellier – France. All consecutive adult diabetic patients admitted to that unit during the study period were assessed for eligibility. We included patients with type 1 or 2 DM who received statin treatment for at least three months, had at least one fasting blood lipid profile available during hospitalization, and were classified at very high risk according to the last ESC guidelines [7]. Patients with DM were considered at very high CV risk when they had a major risk factor such as smoking, hypertension or dyslipidemia, or a target organ damage such as proteinuria [7]. Patients were considered as having DM if they were currently on diabetes therapy. Patients with fibrate treatment were not included. Patients with end-stage renal disease (stage 5 chronic kidney disease) were not included due to the lack of evidence of statin treatment for CV management in this population. Patients with elevated triglycerides (>4.5 mmol/L) were excluded due to the impossibility of using the Friedewald formula.

Our observational study follows the World Medical Association's Declaration of Helsinki and meets the requirements of the MR003 procedure of the "Commission Nationale de l'Informatique et des Libertés" (compliance statement N° 1984895). Indeed, this study was strictly observational as all treatments, examinations and blood samples were performed in routine medical care. As such, the study served to comprehensively document current practices in patients with DM.

2.2. Data collection

Data on age, sex, tobacco smoking, body mass index, hypertension (treatment of previously diagnosed hypertension or blood values > 140/90 mm Hg), presence and type of CVD (coronary artery disease (CAD), stroke and transient ischemic attack (TIA), peripheral arterial disease), were collected at admission. LDL-C levels were calculated with the Friedewald formula, and glomerular filtration rate according to the CKD-EPI formula. Blood samples were taken within 24 h of hospitalization admission. Microalbuminuria, diabetic retinopathy and CVD definitions and diagnosis were conform to ADA guidelines [12].

Information on the name and daily dose of lipid lowering drugs (statins and/or ezetimibe) at admission was documented. Statin intensity was classified in three categories according to expected LDL-C reductions: high (rosuvastatin 20 mg, atorvastatin 40 and 80 mg by day), moderate (rosuvastatin 5 and 10 mg, atorvastatin 10 and 20 mg, fluvastatin 80 mg, simvastatin 20 and 40 mg, pravastatin 40 mg by day) and low intensity (pravastatin 10 and 20 mg, fluvastatin 40 mg and simvastatin 10 mg by day) for respectively expected reduction of ≥50%, 30–49% and <30%, according to ESC guidelines [7,13]. Data were collected by clinical pharmacist.

2.3. Cardiovascular risk classification and LDL-C target value attainment

CV risk level and LDL-C target values were defined according to 2011 and 2016 ESC guidelines [7,13]. Both 2011 and 2016 guidelines have been used because the 2016 update has been published during our inclusion period. Proportion of very high-risk patients and LDL-C target attainment were compared between 2011 and 2016 ESC guidelines. Patients classified as being at very high-risk had LDL-C target values of <1.8 mmol/L. The distance to the LDL-C target was calculated for patients who did not achieve target value.

2.4. Factors associated with not reaching LDL-C target

Patients were divided into two subgroups depending on whether they achieved LDL-C target (<1.8 mmol/L) or not (≥1.8 mmol/L). The following variables were thus considered: age, sex, BMI, history of CVD (CAD, stroke or TIA, peripheral artery disease), HDL-C level, statin intensity (low vs moderate intensity and low vs high intensity) and ezetimibe treatment.

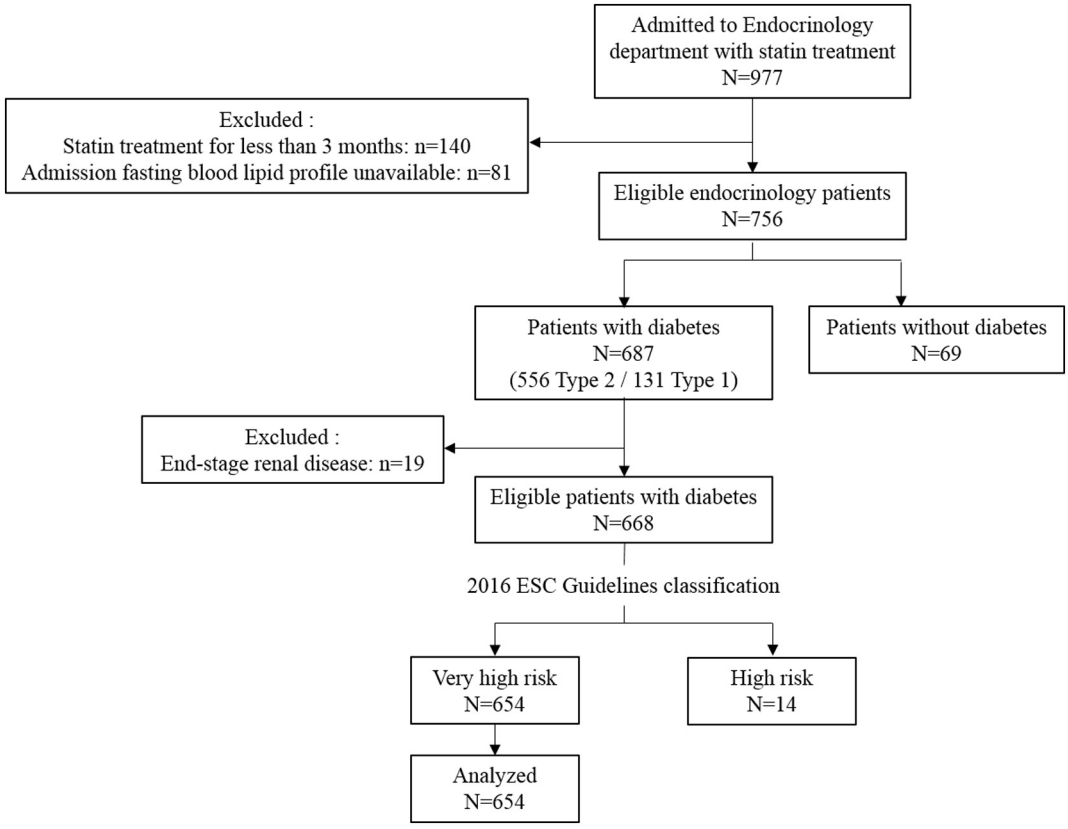

Fig. 1. Flow chart of the study population.