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Original article

The decreased achievement of therapeutic goal in lipid lowering therapy in obese and diabetic patients in Poland

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ABSTRACT

Background: Statins are used to reduce a cardiovascular risk. However, the effectiveness of the therapy in many cases remains unsatisfactory. Therefore, the aim of this study was to evaluate the influence of obesity and diabetes on the achievement of therapeutic goal in lipid-lowering therapy in patients with a various cardiovascular risk in the daily clinical practice.

Methods: This study was conducted on the basis of questionnaires obtained from 7018 patients (41.4% obese, 65.9% viscerally obese and 25.3% diabetics) treated with statins for at least three months. The effectiveness of the treatment was assessed in a subgroup of 3218 patients with a full lipid profile.

Results: The LDL-cholesterol target, adjusted for cardiovascular risk, was obtained by 8.1% of patients, less frequently by those with a very high risk of a cardiovascular disease (3.7%), obesity (5.5%), visceral obesity (5.5%) and the type 2 diabetes (5.3%). The obese patients with type 2 diabetes were the least likely to reach the target (3.0%). Male gender, age, the body mass index (BMI) ≥ 28 kg/m², visceral obesity, type 2 diabetes, and a low/moderate statin dose prescription were independent factors decreasing the chance of reaching the low-density lipoprotein (LDL) cholesterol target.

Conclusions: 1. The prescribed statin doses do not fully explain the lower frequency of achieving the recommended target in a lipid-lowering therapy in the obese patients and the diabetics.

2. In the daily clinical practice the doses of statins are frequently insufficient and not adjusted for a cardiovascular risk.

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Introduction

Obesity and particularly diabetes are well established disorders contributing substantially to the pathogenesis and progression of cardiovascular disease (CVD). Both diseases, along with dyslipidemia, are considered the main modifiable risk factors for CVD. Overwhelming evidence indicates that lipid lowering therapies, particularly the treatment with statins, improve cardiac disease outcomes. According to large clinical trials, such as the JUPITER study, the use of statins reduces the risk of a cardiovascular primary end-point by 44% with a simultaneous 50% reduction in the low-density lipoprotein (LDL) cholesterol level (when treated with rosuvastatin) [1].

A recent meta-analysis showed that up to 85% of the change in the total cholesterol level of populations during the last decade may be attributed to the use of statins [2]. However, in many patients the effectiveness of statin therapy remains unsatisfactory. According to the results of the REALITY study [3] and the TARGET TANGIBLE trial [4], only 40–60% of the patients receiving statin therapy achieved the recommended LDL cholesterol targets. The low effectiveness of statin treatment observed in the clinical trials is even more expressed in the survey studies [5].

Our recent study demonstrated that the effectiveness of the lipid-lowering therapy with statins decreased proportionally to the increase of the body mass index (BMI) [5]. Thus, overweight and obesity may be considered as independently associated with the worse LDL-cholesterol-lowering therapy outcome. According to the recent observation by Halava et al. [6], obesity is not a predictor for poor adherence to the therapy regimen. Therefore, one of the hypotheses is that the doses of statins routinely administered are too low in obese patients.

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Interestingly, a retrospective cohort study conducted by Nag et al. revealed that non-diabetic patients with cardiovascular disease were more likely to achieve LDL-cholesterol goal compared to diabetic patients (71.2% vs. 51.8%) [7]. The ARETAEUS study results showed that only 20% of the diabetic patients in Poland had the LDL-C levels below 2.5 mmol/l [8]. The explanation for this observation is complex, but this finding implies that diabetes itself may influence the effectiveness of a lipid-lowering therapy. Therefore, the aim of this study was to evaluate the influence of obesity and diabetes on the achievement of the therapeutic goal in a lipid lowering therapy in patients with various cardiovascular risks in daily clinical practice.

Material and methods

Two-hundred-two cardiologists participated in the survey (conducted in February and March 2013) after signing a declaration of willingness to participate in the study. Seven thousand and eighteen patients treated with statins for at least three months were included. The study was conducted in Poland in February and March 2013. The only exclusion criterion was the inability to obtain the data necessary to fill in the study questionnaire. The study procedures were in accordance with the ethical standards and the Helsinki Declaration of 1975, as revised in 2008 in Seoul. The questionnaire-based survey did not fulfil the criteria of a medical experiment and thus did not require a bioethics committee approval. All the patients involved were informed about the nature of the study and agreed to participate.

The investigators (participating cardiologists) completed the questionnaire on the basis of medical records (without the patient's personal details) from the routine ambulatory examination.

The first part of the questionnaire included the demographic data (sex, age, place of residence, education), the anthropometric data (weight, height, waist, and left arm circumference), two blood pressure measurements, and additionally, the questions about the life style (physical activity, smoking habits), and the occurrence of cardiovascular diseases (coronary artery disease, past myocardial infarction, past revascularization procedures, heart failure, arrhythmias, past stroke or transient ischemic attack), and selected comorbidities [chronic kidney disease, type 1 diabetes (with coexisting albuminuria and chronic kidney failure), type 2 diabetes, obesity, visceral obesity, hypertension (both poorly and well controlled)].

The second part of the questionnaire included notes from an interview concerning the lipid profile carried out within the preceding 3 months (with fields for entering total cholesterol, LDL, high-density lipoprotein, triglycerides values), and the use of statins, with their doses. In addition, there were questions concerning the changes in pharmacotherapy and the initiation/modification of the statin dose.

Data analysis

Overweight and obesity were classified according to the World Health Organization criteria [9]. According to the widely accepted WHO criterion, a patient is considered obese if the BMI is equal or greater than 30 kg/m². Obesity is categorized in three categories: mild (BMI 35 > BMI ≥ 30 kg/m²), moderate (40 > BMI ≥ 35 kg/m²) and morbid obesity (as BMI ≥ 40 kg/m²). Visceral obesity was defined according to the International Diabetes Federation 2005 criteria, as waist circumference ≥ 94 cm for European men and ≥ 80 cm for European women [10].

The overall 10-year risk of a cardiovascular event was assessed on the basis of the recommendations of the European Society of Cardiology for high risk countries from 2011 [11] and Pol-SCORE

2015 [12]. The very high-risk group included the patients diagnosed with atherosclerosis, type 1 or 2 diabetes accompanied by albuminuria, severe chronic kidney disease (CKD) (with eGFR <30–59 ml/min/1.73 m²), or 5-year risk SCORE ≥ 10%. The high-risk group included those with severe hypertension or with type 1 or 2 diabetes but without albuminuria, and those with moderate CKD (with eGFR 30–59 ml/min/1.73 m²), or 5-year risk SCORE <10% but ≥ 5%.

In the other cases it was advised to calculate the risk, taking into account the total cholesterol level before the initiation of a statin therapy, systolic blood pressure, smoking status, age and sex.

The targets for LDL-cholesterol levels were assumed as follows: <3.0 mmol/l for the patients with small (<1%) or moderate (1–5%), <2.6 mmol/l for the subjects with high (5–10%) and <1.8 mmol/l for those with very high overall 10-year risk of a cardiovascular event [11].

The statin doses were stratified as low or moderate (< 40 mg of simvastatin or atorvastatin, <20 mg of rosuvastatin) or high and very high (at least 40 mg of simvastatin or atorvastatin, at least 20 mg of rosuvastatin). Patients treated with ezetimibe were not included into the analysis, due to a low number of cases.

Statistical analysis

The statistical analysis was performed using the software STATISTICA 10.0 PL (StatSoft Polska, Kraków, Poland) and MedCalc 12.3.0.0. (Mariakerke, Belgium). The qualitative data are presented as an average percentage, while the quantitative data as the mean with standard deviation or 95% confidence interval. The scheduled qualitative variables were compared using χ^2 and χ^2 test for trend. The ANOVA and *post hoc* Tukey test were used for the comparison of variances of the variables.

Receiver operating characteristic analysis was applied to estimate BMI value that were increasing the risk of not achievement of the LDL goal in lipid lowering therapy, adequate for individual cardiovascular risk.

Logistic regression analysis was used to calculate odds risks for factors explaining the achievement the goal in lipid lowering therapy adequate for individual cardiovascular risk; *p* values < 0.05 were considered statistically significant.

Results

Study group characteristics

The demographic characteristics of the 7018 outpatients on statins, treated by a cardiologist are shown in Table 1. The average age was 62 ± 10 years, 37.1% of the respondents were over 65 years of age. Urban dwellers accounted for 64.5% of the respondents, 21.0% were university educated. 41.4% of the respondents were obese according to the World Health Organization criteria and 65.9% according to the International Diabetes Federation criteria. The prevalence of sedentary lifestyle was overall 67.4%, including 72.4% of obese patients.

The prevalence of comorbidities is presented in Table 2. Type 2 diabetes was diagnosed in 1777 (25.3%) of the patients, with the highest prevalence among those obese (34.2%). Physicians had diagnosed obesity only in 45.6% of the obese patients. A high and very high, 10-year cardiovascular risk, was assessed in 12.4% and 77.6%, respectively.

Statin therapy

The most commonly used statin was atorvastatin (44.7%), followed by simvastatin (30.3%), and rosuvastatin (25.0%). No other

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