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Are the ESC guidelines on lipid-lowering treatment implemented in morbidly obese patients qualified for bariatric surgery?

Short title: Lipid-lowering treatment in patients with morbid obesity

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INTRODUCTION

The primary aims of atherosclerotic cardiovascular disease (ASCVD) prevention are to reduce morbidity, mortality, and increase life expectancy [1]. An important aspect of this prevention is the control of apo-B-containing lipoproteins, which contribute to the induction and progression of ASCVD [1]. Prompt diagnosis and implementation of lipid-lowering treatment at every stage of dyslipidemia results in a better prognosis and lowers the risk of cardiovascular events [1, 2].

Adiposity is another major risk factor of ASCVD. This condition increases the chance of developing cardiovascular disease (CVD) by promoting dyslipidemia, diabetes mellitus (DM), and other disturbances [1]. According to recent reports, 12.5% of the world's population is obese [3]. This number is doubled in Poland [4].

Our aim was to assess physicians' adherence to the latest guidelines on primary CVD prevention. To address this problem, we focused on the pharmacological treatment of dyslipidemia in morbidly obese patients before bariatric surgery. Our objective was to assess CVD risk, hypolipidemic agents' introduction indications, and their efficacy among the aforementioned individuals.

METHODS

We enrolled consecutive patients 35 years of age or older, with morbid obesity, who had been admitted to the surgery ward to undergo bariatric surgery and agreed to participate in the study. The recruitment took place between December 2021 and April 2022. The exclusion criteria were secondary CVD prevention, chronic kidney disease, and familial hypercholesterolemia.
Medical records were used to characterize patients.
The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the institutional ethics committee. Informed consent was obtained from each study participant.
IBM SPSS Statistics for Windows, Version 28.0. (Armonk, NY:IBM Corp) software was used for statistical analysis. Continuous data values were presented as mean (standard deviation [SD]) or median (interquartile range [IQR]), qualitative data as the number and percentage. The χ^2 test and Fisher-test were used to compare qualitative data, while the Student's t-test (for data with normal distribution) and the Mann–Whitney U-test (for variables with other than normal distribution) were used for quantitative data. Continuous variables were first checked for normal distribution by the Shapiro-Wilk-test. For all tests a *P*-value less than 0.05 was considered significant. A detailed description of the study methods is presented in Supplementary material.

RESULTS AND DISCUSSION

We enrolled 57 patients with morbid obesity (n = 41; 71.9% women) at a median (IQR) age of 46 (38–51) years. More than one-fourth (n = 15; 26.3%) had DM. Detailed basic characteristics are presented in Supplementary material, *Table S1*. The mean (SD) non-high-density lipoprotein cholesterol (non-HDL-C) level was 3.16 (0.11) mmol/l, low-density lipoprotein cholesterol (LDL-C) 2.66 (0.09) mmol/l, median (IQR) serum concentration of triglycerides (TG) was 1.28 (0.94–1.56) mmol/l, total cholesterol 4.3 (3.8–4.9)mmol/l. Ten patients (17.5%) were smokers or have quitted during the last stage of surgery preparations (≤3 months before surgery). Half of the patients had high CV risk (n = 29; 50.9%), followed by low-moderate (n

= 26; 45.6%) and very high (n = 2; 3.5%). More than one-fifth (n = 12; 21.1%) of study participants had hypercholesterolemia diagnosed before enrollment. Out of these, ten persons (17.5%) had some sort of pharmacological treatment. Most of them were statins-only users (n = 6; 60% of patients on hypolipidemic treatment), two (20%) were on fibrates, one (10%) had statin and fibrate, and one (10%) took statin and ezetimibe. However, only one of those patients had an LDL-C level within normal limits, while all others could have their treatment intensified. Two patients (3.5%)(with dyslipidemia diagnosed earlier) had no treatment introduced, while requiring it.

Dyslipidemia was newly diagnosed in other 15 patients. Altogether, almost half of the study population (n = 27; 47.4%) had hypercholesterolemia, but was on none or insufficient treatment. This number included 5 (8.8%) persons with hypertriglyceridemia. None of the previously mentioned met the exclusion/discontinuation criterion of statins treatment, which is creatine kinase >4 times the upper limit of normal, and only 4 (14.8% of lipid-lowering therapy needers) could not have taken these drugs because of alanine aminotransferase level, which was >3 times the upper limit of normal [2].

As shown in Table 1, patients that required dyslipidemia treatment had higher levels of alanine aminotransferase, non-HDL-C, and LDL-C. Moreover, the group that needed hypolipidemic treatment consisted mostly of men.

Although there is a large number of previously published papers on lipid profile, and pharmacological lipid-lowering treatment in morbidly obese patients before bariatric surgery, they do not provide data on undiagnosed lipid metabolism disorders, and a number of untreated patients [7–9]. Our study is the first to show this information.

In our work, the percentage of morbidly obese patients with hypercholesterolemia before bariatric surgery is comparable to the ones presented in other research, although a fraction of participants with hypertriglyceridemia, which we observed, was significantly lower compared to 24% and 53% reported in the literature [5, 8, 9]. This disproportion might partially result from the diagnostic criterion we based on, when setting the threshold value of TG: 2.3 mmol/l [1].

The average levels of LDL-C and TG presented in this paper (2.66 and 1.28, respectively) are lower than the values reported in a similar studies from Austria (3.12 and 1.78) [6], Singapore (3.05 and 1.66) [7] and the US (2.88 and 1.74) [10]. On the contrary, serum levels of non-HDL-C in the Austrian work (3.9), and total cholesterol shown in the Singaporean investigation (4.9) were lower than those quoted in our paper (3.16 and 4.3, respectively). All above values are presented in mmol/l. Further, the fraction of perioperative statin users ratio observed in our

study is much lower in comparison to the results reported in American works (10.5% vs. 24.5% and 34%) [10, 12].

The outcome of our investigations, revealing insufficiencies in pharmacological treatment of dyslipidemia in morbidly obese patients before bariatric surgery, calls for clarification. One factor that might have influenced the outcomes was COVID-19 pandemic, which reduced accessibility of healthcare. Another reason may be the patients, not taking the prescribed medications. In any case, our results should encourage all physicians involved in morbidly obese patients' care to active screening for dyslipidemia and regular evaluation of lipid-lowering treatment effectiveness. There are three main reasons why above mentioned checks should be performed particularly in individuals qualified for bariatric surgery. Firstly, the process of preparing for surgery should last 6–12 months, so there is plenty of time to introduce effective treatment before hypothetically more effective intervention [13]. Secondly, quite a considerable number, reaching 40% of post-bariatric patients, do not demonstrate dyslipidemia remission. What is more, its relapse rate may come up to 24% [14]. Lastly, patients on preoperative statins may have a higher rate of DM and hypertriglyceridemia remission [11,14].

The main limitation of our research is the fact that the study was conducted in one bariatric center, and the enrolled group was relatively small. Moreover, we did not have data regarding target organ damage in patients with DM, which might have impaired their CV risk assessment. Nevertheless, if we had possessed this information, we could only have assigned such patients to the higher CV risk group, which would support the outcomes.

In conclusion, our study is the first to show that morbidly obese patients before bariatric surgery may be underdiagnosed and undertreated for dyslipidemia. These findings, if confirmed by further research involving a larger number of clinical centers, would indicate a need for revisiting the clinical practices applied to patients qualified for bariatric surgery.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

Conflict of interest: None declared.

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Table 1. Comparison between hypolipidemic treatment groups in terms of basic characteristic and selected parameters			
	Did not require lipid-lowering treatment (n = 30)	**Require lipid-lowering treatment (n = 27)**	***P*-value**
Age, years, median (IQR)	45.50 (39.00–51.00)	48.00 (37.00–52.00)	0.88
Female, n (%)	25 (83.3)	16 (59.3%)	0.04
BMI, kg/m^2, median (IQR)	40.41 (37.13–46.65)	42.52 (38.57–47.40)	0.24
Maximal noted body weight, kg, median (IQR)	126.50 (108.00–141.00)	130.00 (120.00–164.00)	0.23
Waist circumference, cm, median (IQR)	111.00 (108.00–128.00)	125.50 (114.00–132.00)	0.01
Hip circumference, cm, median (IQR)	132.00 (121.00–145.00)	133.50 (122.00–139.00)	0.64
Waist/hip ratio, mean (SD)	0.89 (0.02)	0.93 (0.02)	0.09
Active smoker, n (%)	0 (0%)	10 (37.0%)	<0.001[1]
SBP, mm Hg, mean (SD)	132.81 (2.18)	137.26 (2.73)	0.20
DBP, mm Hg, mean (SD)	82.98 (1.61)	84.19 (1.37)	0.57
CVD risk, %, median (IQR)	2 (1–2)[2]	4 (3–5.25)[3]	<0.001
ALT, U/l, median (IQR)	41.00 (28.00–59.00)	56.00 (46.00–77.00)	0.02
Total cholesterol mmol/l, mean (SD)	4.18 (0.16)	4.55 (0.14)	0.09
HDL-C mmol/l, median (IQR)	1.15 (1.07–1.37)	1.11 (1.01–1.21)	0.24
Non-HDL-C, mmol/l, mean (SD)	2.94 (0.15)	3.41 (0.14)	0.02

LDL-C, mmol/l, mean (SD)	2.49 (0.14)	2.85 (0.11)	0.05
TG, mmol/l, median (IQR)	1.27 (0.96–1.59)	1.31 (0.92–1.56)	0.94
Glucose, mmol/l, median (IQR)	5.53 (5.01–6.29)	5.76 (5.18–6.64)	0.37
HBA1C, %, median (IQR)	5.60 (5.40–5.90)	5.90 (5.60–6.40)	0.02
CK, U/l, median (IQR)	211.50 (152.00–301.00)	203.00 (151.00–260.00)	0.81
Creatinine, µmol/l, mean (SD)	71.82 (1.99)	72.14 (3.13)	0.93
GFR, ml/min/1.73 m^2, mean (SD)	88.24 (3.25)	90.85 (3.50)	0.59

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CK, creatine kinase; CVD, cardiovascular disease; DBP, diastolic blood pressure; GFR, glomerular filtration rate; HbA1C, Glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Non-HDL-C, non-high-density lipoprotein cholesterol; SBP, systolic blood pressure; TG, triglycerides.

[1]More than 20% of expected counts were less than 5. [2]CVD risk calculated for 27 individuals. [3]CVD risk calculated for 17 individuals