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Original Article

Bariatric surgery improves lipoprotein profile in morbidly obese patients by reducing LDL cholesterol, apoB, and SAA/PON1 ratio, increasing HDL cholesterol, but has no effect on cholesterol efflux capacity

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KEYWORDS:
Bariatric surgery;
Obesity;
Lipoprotein particle subclasses;
Paraoxonase/arylesterase 1 (PON1);
Serum amyloid A (SAA);
Cholesterol efflux capacity

BACKGROUND: Bariatric surgery has been shown to reduce cardiovascular events and cause-specific mortality for coronary artery disease in obese patients. Lipoprotein biomarkers relating to low-density lipoprotein (LDL), high-density lipoprotein (HDL), their subfractions, and macrophage cholesterol efflux have all been hypothesized to be of value in cardiovascular risk assessment.

OBJECTIVES: The objective of this study was to examine the effect of a lifestyle intervention followed by bariatric surgery on the lipid profile of morbidly obese patients.

METHODS: Thirty-four morbidly obese patients were evaluated before and after lifestyle changes and then 1 year after bariatric surgery. They were compared with 17 lean subjects. Several lipoprotein metrics, serum amyloid A (SAA), serum paraoxonase/arylesterase 1 (PON1), and macrophage cholesterol efflux capacity (CEC) were assessed.

RESULTS: Average weight loss after the lifestyle intervention was 10.5% and 1 year after bariatric surgery was 33.9%. The lifestyle intervention significantly decreased triglycerides (TGs; −28.7 mg/dL, $P < .05$), LDL cholesterol (LDL-C; −32.3 mg/dL, $P < .0001$), and apolipoprotein B (apoB; −62.9 μg/mL, $P < .001$). Bariatric surgery further reduced TGs (−36.7 mg/dL, $P < .05$), increased HDL cholesterol (+12 mg/dL, $P < .0001$), and reductions in LDL-C and apoB were sustained. Bariatric surgery reduced large, buoyant LDL ($P < .0001$), but had no effect on the small, dense LDL. The large HDL subfractions increased ($P < .0001$), but there was no effect on the smaller HDL

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subfractions. The ratio for SAA/PON1 was reduced after the lifestyle intervention ($P < .01$) and further reduced after bariatric surgery ($P < .0001$). Neither the lifestyle intervention nor bariatric surgery had any effect on CEC.

CONCLUSIONS: Lifestyle intervention followed by bariatric surgery in 34 morbidly obese patients showed favorable effects on TGs, LDL-C, and apoB. HDL cholesterol and apoA1 was increased, apoB/apoA1 ratio as well as SAA/PON1 ratio reduced, but bariatric surgery did not influence CEC.

Introduction

Obesity, defined as a body mass index (BMI) > 30 kg/m^2, is a growing health problem in large parts of the world. Worldwide obesity has doubled since 1980, and the prevalence of obesity in adults has passed 20% in most Western countries.[1] Similar increases in childhood obesity predict that we have not yet seen the peak of this epidemic.[2] Obesity is associated with known cardiovascular risk factors such as hypertension, dyslipidemia, type II diabetes, and chronic inflammation.[3] An increased risk of morbidity and mortality from cardiovascular disease (CVD) is well documented in obese patients.[4]

Bariatric surgery is considered a safe and effective treatment for obesity,[3] usually recommended to patients with severe obesity, defined as a BMI >40 kg/m^2 or BMI >35 kg/m^2 in the presence of substantial comorbidities such as hypertension, diabetes, and obstructive sleep apnea. Bariatric surgery results in significant and sustained weight loss and reduces all-cause mortality and cause-specific mortality from coronary artery disease.[5]

The typical dyslipidemia observed in obese patients consists of elevated fasting and postprandial triglycerides (TGs), reduced high-density lipoprotein cholesterol (HDL-C) and normal or just slightly elevated low-density lipoprotein cholesterol (LDL-C).[3] These routine lipoprotein biomarkers fail to identify a significant proportion of patients at risk of cardiovascular events,[6] and there has been intensive research into whether different advanced lipoprotein testing methods can improve cardiovascular risk prediction. LDL and HDL particles are heterogeneous with respect to size, density, composition, and function. Several LDL and HDL metrics have been investigated, with the most common being total and subfraction particle numbers, sizes, and lipid content. Small, dense LDL (sdLDL) has been associated with increased cardiovascular risk, obesity, and diabetes. sdLDL biomarkers include LDL diameter or phenotype, particle number (sdLDL-P), or cholesterol content (sdLDL-C).[7–9] Despite over 3 decades of research, the clinical utility of LDL sub-fractionation continues to be debated.[6]

Cholesterol efflux capacity (CEC), the ability of HDL to accept cholesterol from macrophages, a step in reverse cholesterol transport, has been inversely associated with cardiovascular events.[10] The relevance of HDL subfractions and subclasses as markers for HDL-related risk is uncertain,[11] but recent studies have shown that small, dense HDL particles seem to be more efficient in mediating ABCA1-mediated cholesterol efflux from macrophages.[12] Other aspects of HDL functionality include Q8 the ability to mitigate oxidative and inflammatory arterial wall responses. Paraoxonase-1 (PON1) is an HDL-associated enzyme capable of preventing LDL oxidation, and reductions in PON1 activity are believed to lead to dysfunctional HDL.[13] Serum amyloid A (SAA) is an acute-phase protein that increases during inflammation and impairs the anti-inflammatory properties of HDL, possibly by replacing protective proteins in HDL.[14] An increased ratio of SAA/PON1 activity has been proposed as a possible marker for dysfunctional and pro-inflammatory HDL.[15]

The effect of bariatric surgery on lipoprotein composition and function is largely unknown. Furthermore, the mechanisms through which bariatric surgery affects morbidity and mortality are not fully understood. We hypothesized that lifestyle changes followed by bariatric surgery would induce a more favorable lipoprotein profile in morbidly obese patients and, therefore, examined the effects of bariatric surgery on TGs, LDL-C, and HDL-C, apolipoprotein (apo) B, apoA1, apoB/apoA1-ratio, HDL and LDL subfractions, and HDL functions measured by SAA, PON1 activity, and macrophage CEC.

Materials and methods

Study participants and experimental design

In this prospective study, we included 34 patients admitted to the Regional Centre for Treatment of Morbid Obesity, Nordland Hospital, Norway. The patient population has been described previously.[16] Briefly, inclusion criteria in the morbidly obese group were as follows: aged >18 years, BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with significant comorbidity such as hypertension, type II diabetes mellitus, or sleep apnea. The patients underwent lifestyle changes for a mean period of 3 months before bariatric surgery. The control group consisted of 17 subjects