

Patients with Type 2 Diabetes Mellitus have a Lipoprotein Subpopulation associated with Insulin Resistance and Inflammation

Katarzyna Roszek*

Department of Molecular Biology, Silesia, Poland

Abstract

The numerous subpopulations of plasma lipoproteins, each of which has a distinct number and size of particles, are not adequately represented by the standard lipid panel. In order to determine whether certain lipoprotein subpopulations are associated with insulin resistance and inflammation markers, we sought to quantify lipoprotein subpopulations in patients with type 2 diabetes mellitus (T2DM). 57 T2DM patients ranging in age from 61.14 to 9.99 years were included in the study; HbA1c, 8.66 \pm 1.60%; on average, BMI of 35.15 minus 6.65 kg/m2). Nuclear magnetic resonance spectroscopy was used to determine the size and count of plasma lipoprotein particles. Multi-regression analysis was used to investigate the connection between scores for glycoprotein acetylation (GlycA) and lipoprotein in resistance (LPIR). The largest numbers and sizes of VLDL and HDL particles were found to be most correlated with LPIR in stepwise regression analysis (R2 = 0.960; However, there was a correlation between HDL and VLDL particle concentrations and GlycA (R2 = 0.190; All sizes of lipoproteins, as well as small and large VLDL particles, independently predicted LPIR in adjusted multi-regression analysis (p = 0.0001), whereas only a small number of LDL particles independently predicted GlycA. Conventional markers HbA1c and Hs-CRP did not have a significant relationship with lipoprotein subpopulations. Based on our findings, we hypothesize that by keeping an eye on the changes caused by insulin resistance in T2DM subpopulations of lipoproteins, we might be able to find novel biomarkers that could be used in clinical intervention.

Keywords: Inflammation; Lpir; Glyca; Lipoprotein Subpopulations; Lipids; Hypertension; Coronary artery Disease

Introduction

Type 2 diabetes mellitus (T2DM) is characterized by abnormalities in plasma lipids and lipoproteins, such as decreased high-density lipoprotein (HDL) cholesterol, elevated triglycerides, and a predominance of small dense low-density lipoprotein (LDL). Despite taking multiple lipid-lowering medications to reach their normal target levels of LDL cholesterol, many diabetics may continue to experience these abnormalities. Insulin resistance has a significant impact on both the size of lipoproteins and the concentrations of subpopulation particle concentrations of circulating plasma lipoproteins [1]. Numerous studies have consistently demonstrated that atherogenic lipoprotein particle concentrations, specifically levels of small dense LDL and triglyceriderich lipoprotein remnants, are predictive of coronary artery disease (CAD), despite the presence of other known risk factors.

Dyslipidemia and inflammatory status have been linked in numerous studies. Inflammatory cytokines are the cause of most proatherogenic alterations in lipid metabolism. As a result of these changes, HDL cholesterol's anti-inflammatory, antioxidant, and reverse cholesterol functions are impaired. Two systemic inflammatory markers, white blood cells and high sensitivity C-reactive protein (Hs-CRP), are also closely linked to atherogenic lipoprotein subfractions in CAD patients [2-5].

When compared to a standard lipid panel, changes in lipids and lipoproteins in diabetic dyslipidemia do not always provide the complete information necessary to evaluate the effects of insulin resistance and the risks of cardiovascular disease (CVD) in diabetic patients. By demonstrating the significance of unconventional lipid parameters in predicting the risk of diabetes, a recent longitudinal study of 15,464 non-diabetic participants demonstrated the need for a better characterization of a comprehensive lipid profile evaluation in diabetics. Over the past few decades, numerous analytical assays have been developed to distinguish plasma lipoproteins according to their number, composition, and size **[6**]. As new NMR spectroscopy assays were developed, numerous studies focused on the relationship between lipoprotein subfractions and cardiovascular outcomes.

The novel composite metabolomic biomarker known as the lipoprotein insulin resistance score (LPIR) identifies various aspects of insulin resistance through the use of high throughput NMR. Six lipoprotein particles, including VLDL, LDL, and HDL, make up this weighted score. Also important are the particle concentrations of large VLDL, small LDL, and large HDL, which are all more strongly associated with insulin resistance than any other subclass [7]. The LPIR score was found to be linked to the incidence of type 2 diabetes (T2DM) independently of other known risk factors for cardiovascular disease when used to assess insulin resistance and the risk of type 2 diabetes (T2DM).

Population and Method of the Study

King Abdulaziz Hospital (KAH) and the Ministry of National Guard-Health Affairs (MNGHA) in Al-Ahsa, Kingdom of Saudi Arabia, recruited 57 T2DM patients from January 2020 to April 2021. With a wide range of specialties, the MNGHA is a well-known accountable health system that receives funding from the government and provides exceptional patient care. It has cutting-edge technology for clinical care, education, and research in addition to an established,

*Corresponding author: Katarzyna Roszek, Department of Molecular Biology, Silesia, Poland, E-mail: Ros@zek.gamil.com

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HIMSS INFRaM-6-maturity information system infrastructure. The MNGHA Institutional Review Board approved the study's protocol (IRB protocol number IRBC/1972/18) after each participant gave written informed consent. At the beginning of the study, patients who met one or more of the following criteria were dropped: This group included individuals who were on chronic renal replacement therapy (hemodialysis, peritoneal dialysis, or transplantation), had a history of active cancer (with the exception of basal cell carcinoma) within the previous five years (prostatic cancer within the previous five years), and had a history of acute infection or fever [8]. Systemic and other autoimmune diseases of lupus erythematosus Diabetes: subjects who had a fasting glucose level of less than 126 mg/dL (7 mmol/L), were taking a T2DM medication, and had a HbA1c of less than 6.5%. Any first-degree relative with a T2DM diagnosis was presumed to have a T2DM family history. Dyslipidemia: subjects whose systolic or diastolic blood pressure was less than 90 mmHg and who were taking antihypertensive medications. subjects whose fasting lipid profile contained total cholesterol greater than 200 mg/dL or LDL greater than 70 mg/dL. subjects whose dyslipidemia medication had been previously taken. CKD: subjects whose dipstick urine test used the diet modification equation for renal disease (MDRD) revealed proteinuria of less than 2+ or an eGFR of less than 90 mL/min [9,10].

Discussion

Nuclear magnetic resonance (NMR) is one method that has been extensively utilized to investigate changes in the lipoprotein profile in depth. However, the nature and duration of the disease, patient age, and results from diverse ethnic populations were inconsistent. Numerous studies have been conducted over the past few decades on a number of lipid-lowering medications, focusing not only on the reduction in LDLc but also on the size of LDL particles. This has increased the medication's clinical value beyond that of a standard lipid panel. the rise in small, low-density LDL. Despite the best lipid-lowering treatments, such as statins, many diabetic patients still face a high risk of cardiovascular disease (CVD) in the long run. This is because the condition is getting worse because of other factors like high hepatic secretion of large triglyceride-rich VLDL, poor VLDL clearance, and low HDL particles.

Despite the fact that universal advanced lipoprotein profiling still faces some challenges and limitations, comprehensive NMR-derived lipoproteins analysis is a reliable and powerful tool that can expand diagnostic value and disease management when interpreting results of lipid panel and lipoproteins disturbance in T2DM patients.

Conclusions

Advanced NMR-derived lipoproteins showed that VLDL and HDL were the best predictors of T2DM patients' insulin resistance scores. LDL and HDL particle sizes were negatively correlated with LPIR but not HbA1c levels, whereas the number and size of large VLDL particles were positively correlated with LPIR. Intriguingly, systemic inflammation is not as good a predictor of insulin resistance as atherogenic lipoprotein subpopulation size and number in T2DM patients. Only small LDL particles were positively correlated with GlycA, a marker for systemic inflammation. Larger prospective longitudinal studies are required to demonstrate that advanced lipoprotein profiling is superior in clinical settings. To identify potential subpopulations of lipoproteins, biomarkers that can be measured to predict and prevent type 2 diabetes will be utilized.

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