among groups according to their sport types, these differences might have affected the correlations in this study. However, the statistical significance remained evident after the adjustment for ethnicity ($p < 0.001$ for LVGLS and $p < 0.001$ for LVGLSR-S).

In conclusion, female university athletes had lower LV volumes, mass, and higher LVEF and strain values than men. LVGLS and LVGLSR-S were significantly decreased along with the increase of cardiovascular demands. The present study demonstrated that there are sex or sports discipline differences in LV mechanics as measured by 2DSTE in highly trained university athletes. Because this was a cross-sectional study, further long-term follow-up studies will be needed to determine whether the reduced strain values reflect subtle myocardial damage and its clinical significance.

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Triglyceride-to-High-Density Lipoprotein Cholesterol Ratio and Vulnerable Plaque Features With Statin Therapy in Diabetic Patients With Coronary Artery Disease

Frequency-Domain Optical Coherence Tomography Analysis

Ongoing cardiovascular risks in patients with type 2 diabetes mellitus (T2DM), despite the use of statins, need additional therapeutic targets. We investigated whether diabetic dyslipidemia, characterized by hypertriglyceridemia and low high-density lipoprotein cholesterol (HDL-C), was associated with plaque features in 267 statin-treated patients with T2DM and coronary artery disease who underwent frequency-domain optical coherence tomography (FD-OCT) within the target vessel for percutaneous coronary intervention.

FD-OCT measures and fasting blood biochemical data were compared in subjects stratified by triglyceride-to-HDL-C ratio tertiles. A generalized estimating equations approach was used to consider the intraclass correlation because of the multiple plaques analyzed within a single patient's data. Multivariate linear regression analyses were performed to identify independent determinants for lipid arc (°) and cholesterol crystal (CC) presence. Receiver-operating characteristic analysis was performed to determine the optimal cutoff value of the triglyceride-to-HDL-C ratio for lipid-rich plaque containing CC. The Institutional Review Board of the Cleveland Clinic (Cleveland, Ohio) approved this retrospective study. All statistical analyses were performed using SPSS version 17.0 software (SPSS, Inc., Chicago, Illinois).

A total of 482 nonculprit and 325 culprit plaques were analyzed within 423 imaged target vessels. Nonculprit and culprit plaques in patients with a higher triglyceride-to-HDL-C ratio exhibited a larger lipid burden and a higher frequency of CC (**Figures 1A and 1B**). Patients with a higher triglyceride-to-HDL-C ratio had a larger total lipid index (1,309.6 mm° vs. 2,933.4 mm° vs. 4,105.6 mm°; $p = 0.005$), by calculating the sum of the lipid index within the entire imaged vessel. After adjusting for age, sex, risk factors, medications, glycosylated hemoglobin (HbA_{1c}), and lipids, the triglyceride-to-HDL-C ratio was an independent determinant of lipid arc

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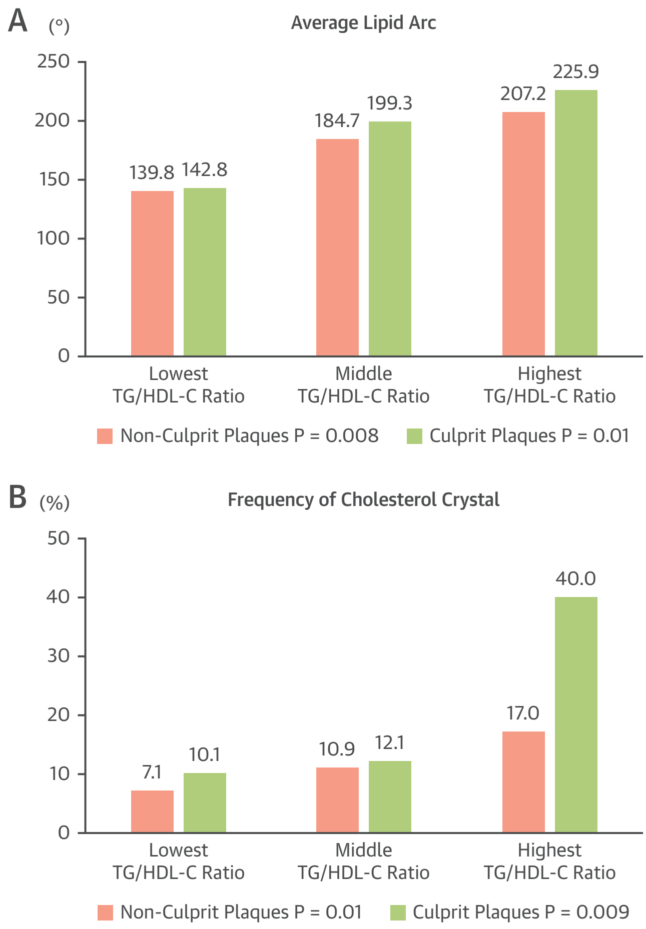
FIGURE 1 Comparison of Plaque Features According to Tertile of Triglyceride-to-HDL-C Ratio



(A) Average lipid arc and **(B)** frequency of cholesterol crystal were compared using 1-way analysis of variance. HDL-C = high-density lipoprotein cholesterol; TG = triglyceride.

(β coefficient = 0.38; p = 0.01) and CC (β coefficient = 0.50; p = 0.008), whereas low-density lipoprotein cholesterol (LDL-C) and HbA_{1c} levels were not associated with these measures. Furthermore, the triglyceride-to-HDL-C ratio was still associated with lipid arc, even in patients with LDL-C <70 mg/dl (p = 0.04) or HbA_{1c} <7.0% (p = 0.03). The optimal cutoff value of the triglyceride-to-HDL-C ratio predicting lipid-rich plaques containing CC was 6.0 (area under the curve: 0.80; sensitivity 87.5%; specificity 80.3%; positive and negative predictive values of 75.0% and 92.3%, respectively; positive and negative likelihood ratio of 4.37 and 0.15, respectively; diagnostic odds ratio of 29.13; Youden index 0.678). During a 2-year observational period, there was a trend toward a higher frequency of cardiovascular events in patients with a higher triglyceride-to-HDL-C ratio (log-rank p = 0.12).

Previous studies have demonstrated the relationship of the triglyceride-to-HDL-C ratio with cardiovascular events, a finding suggesting that triglyceride-to-HDL-C ratio is a potential proatherogenic marker. In the current study analyzing statin-treated subjects with T2DM, the triglyceride-to-HDL-C ratio was associated with vulnerable plaque features, thus providing further evidence for a proatherogenic role of diabetic dyslipidemia even with statin therapy. Mechanistically, hypertriglyceridemia corresponds essentially to an increased content of atherogenic lipoproteins, which enhance the inflammatory response and foam cell formation. A diminished capacity of HDL-mediated cholesterol efflux capacity was observed in parallel with increases in triglyceride content in HDL. These properties could induce the accumulation of substantial amount of lipid materials and CC, thereby promoting plaque vulnerability.

LDL-C levels were not associated with FD-OCT measures in our study. Another study reported vulnerable plaque features in diabetic subjects despite achieving low LDL-C levels (1). Furthermore, small LDL particle concentration, but not LDL-C level, was a significant contributor to diabetic atheroma progression (2). Given that small LDL particles often accompany low HDL-C and elevated triglyceride levels, current observations may reflect the relative importance of mixed dyslipidemia in addition to LDL-C in patients with T2DM.

Subanalyses of large clinical trials and meta-analysis have elucidated the benefit of fibrates in diabetic patients with characteristics of diabetic dyslipidemia. Recently, pemafibrate, a novel peroxisome proliferator-activated receptor alpha modulator, was shown to cause a robust reduction in triglyceride levels and an increase in HDL-C levels when the drug was used with background statin therapy (3). Whether modulating an elevated triglyceride-to-HDL-C ratio with pemafibrate will stabilize diabetic atheroma requires further investigation.

Several caveats should be noted. This is a cross-sectional study, which may have limited our ability to detect causal relationships. FD-OCT imaging was conducted according to operators' discretion. We excluded 110 plaques because of poor image quality. This exclusion may cause selection bias. The relationship of current findings with clinical outcomes remains unknown.

In conclusion, the triglyceride-to-HDL-C ratio, but not LDL-C, was associated with vulnerable plaque features in diabetic subjects with coronary artery disease who were taking statins. These observations may indicate that diabetic dyslipidemia is a potential residual cardiovascular risk.

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A Novel Deep Learning Approach for Automated Diagnosis of Acute Ischemic Infarction on Computed Tomography

Stroke is the fourth leading cause of death and the leading cause of morbidity and long-term disability in adults (1). Early diagnosis of acute ischemic stroke (AIS) in patients is difficult and the need for this early diagnosis will increase as the population ages and acute therapies evolve. Deep learning (DL) is a novel machine learning approach that enables automated extraction and classification of imaging features. This study aims to use DL to enhance our ability to evaluate for AIS while offering both automation and confirmation of a diagnosis.

All patients with AIS admitted to the New York-Presbyterian Hospital/Weill Cornell Medical Center between 2011 and 2014 were prospectively registered in the Cornell Acute Stroke Academic Registry. A total of 114 patients with noncontrast-enhanced computed tomography (CT) scan evidence of acute brain infarction were randomly selected. Board-certified neuroradiologists, blinded to the derivation of the model, annotated the images by marking infarct area to obtain an expert consensus interpretation. Digital Imaging and Communication in Medicine data was split randomly into a training set and test set (80:20). A 3-dimensional multiscale, fully convolutional deep learning neural network was developed and trained on the training set of CT images (2). Neural networks are mathematical models built to recognize patterns in images and predict outcomes based on a predefined ground truth (3). The performance of this model was independently tested using the test set and compared with the expert consensus interpretation. Diagnostic accuracy, sensitivity, specificity, and area under the receiver-operating characteristic curve (AUC) for the DL algorithm were calculated at a voxel and image level on the test set. Computer-generated heat maps were created to denote the possibility of infarct (**Figure 1**).

The mean age of the study sample was 76 $\pm$ 13 years, and 62 (55%) patients were female. Imaging datasets were split for the 114 patients into a training set (n = 92) and a testing set (n = 22). In the training set of 5,888 images, infarction was present in 602 (10.2%) images. In the testing set of 920 images, infarction was present in 130 (14.1%) images. A total of 1.5 billion voxels were used to train the model.

The AUC for the DL algorithm for voxel accuracy was 0.973 (95% confidence interval: 0.972 to 0.974). Diagnostic accuracy, sensitivity, and specificity were 92%, 93%, and 92%, respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 86% and 92%, respectively. The AUC for the DL model for automated diagnosis of infarction at an image level was 0.91 (95% confidence interval: 0.90 to 0.94). The corresponding diagnostic accuracy, sensitivity, and specificity were 88%, 65%, and 91%, respectively. PPV and NPV were 49% and 95%.