UNITED ARAB EMIRATES
MINISTRY OF HEALTH & PREVENTION

الإمارات العربية المتحدة
وزارة الصحة ووقاية المجتمع

The First Scientific Conference on Health and Medical Research in the UAE-5-6 December 2022

PHACTR1 & LPL mediate restenosis risk in CAD patients

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Background and aims: Worldwide, coronary artery disease (CAD) is one of the leading causes of death. Standard treatment options for CAD include revascularization by the implantation of stents or coronary artery bypass grafting (CABG). While stent or CABG continue to be the gold standard treatment for CAD, their long-term failure due to restenosis necessitates further research to enhance the success of these procedures. Restenosis significantly reduces life expectancy and is linked to higher healthcare costs. So far, the etiology of restenosis is still not fully understood. It has been determined that the majority of stenosis risk factors also manifest as restenosis. In this study, we investigated numerous risk factors for restenosis in a cohort of CAD patients and control participants with an emphasis on the genetic foundation of this pathology.

Methods: 5,242 patients were enrolled in this study and were assigned as follows: Stenosis group: 3,570 patients with CAD>50% without a prior stent or CABG, and Restenosis group: 1,672 patients with CAD >50% and prior stent deployment or CABG. The R package was used to process all statistical analyses (R version 4.1.2). Categorical data were compared using the chi-square test, while continuous data were analyzed using one-way ANOVA. After adjusting for age, binomial logistic regression was used to examine the relationship between restenosis and risk factors such T2D, hypertension, hyperlipidemia, and low HDL (defined as < 40 mg/dL), especially among women and men. The association of 44 genetic variations with restenosis was conducted using PLINK 1.9 and allele frequencies among Restenosis and Stenosis groups were reported.

Results: Our findings showed that T2D is linked to a higher incidence of restenosis in women, but hyperlipidemia is a significant risk factor for restenosis, particularly in men. In our patients, the genetic loci rs9349379 (PHACTR1) and rs264 (LPL) were linked to an elevated risk of restenosis. While the LPL variant was linked to an increased risk of restenosis in men, the PHACTR1 variant was primarily linked to an elevated risk in women and diabetics.

Conclusions: Women with elevated blood sugar who have already undergone stents are more likely to require a second stent than women with low blood sugar, and this tendency is much more pronounced in the presence of PHACTR1 polymorphisms. Men who have had stents in the past and who have higher cholesterol levels frequently need to have them deployed again, and this risk is increased by the presence of LPL polymorphisms.

Keyword: PHACTR1, LPL, Diabetes, Restenosis