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Pathogenic classification of LPL gene variants reported to be associated with LPL deficiency

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Abstract:

BACKGROUND: Lipoprotein lipase (LPL) deficiency is a serious lipid disorder of severe hypertriglyceridemia (SHTG) with chylomicronemia. A large number of variants in the LPL gene have been reported but their influence on LPL activity and SHTG has not been completely analyzed. Gaining insight into the deleterious effect of the mutations is clinically essential.

METHODS: We used gene sequencing followed by in-vivo/in-vitro and in-silico tools for classification. We classified 125 rare LPL mutations in 33 subjects thought to have LPL deficiency and in 314 subjects selected for very SHTG.

RESULTS: Of the 33 patients thought to have LPL deficiency, only 13 were homozygous or compound heterozygous for deleterious mutations in the LPL gene. Among the 314 very SHTG patients, 3 were compound heterozygous for pathogenic mutants. In a third group of 51,467 subjects, from a general population, carriers of common variants, Asp9Asn and Asn291Ser, were associated with mild increase in triglyceride levels (11%-35%).

CONCLUSION: In total, 39% of patients clinically diagnosed as LPL deficient had 2 deleterious variants. Three patients selected for very SHTG had LPL deficiency. The deleterious mutations associated with LPL deficiency will assist in the diagnosis and selection of patients as candidates for the presently approved LPL gene therapy.

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