Utility of Achilles Tendon Thickness and DNA Analysis for Diagnosing Familial Hypercholesterolemia

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Objective: Familial hypercholesterolemia (FH) is a common genetic disease characterized by hyper-LDL-cholesterolemia, tendon xanthomas (TXs), and premature coronary heart disease. However, FH is highly underdiagnosed and undertreated. The aim of the present study was to evaluate the efficacy of FH gene DNA analysis and Achilles tendon thickness (ATT) for diagnosing FH.

Methods: Total 1687 FH patients were recruited. In 899 patients, DNA analysis was performed on the FH genes; LDL-receptor (LDLR) and proprotein convertase subtilisin/kexin type 9 (PCSK9) genes. ATT was measured in 1,089 patients, and a thick ATT (≧9.0mm) was diagnosed of Achilles TXs. FH patients (n=161) younger than 20 years were evaluated separately.

Results: The sensitivity of ATT for diagnosing FH (n=1089) was 84.8%. We performed DNA analysis in 899 patients and found 64 LDLR mutations in 738 patients and a PCSK9 gain-of-function mutation (PCSK9 E32K) in 54 patients. Thus, the sensitivity of the DNA analysis in adult FH patients was 738/899 (82.1%). The rate of positive DNA analysis and/or ATT findings in the adult FH was 90.3%. ATT (n=44) and DNA analysis (n=129) were performed in the 161 young hetero-FH patients. DNA mutations were confirmed in 117 patients of 129 patients (sensitivity; 90.7%). ATT was positive in 24 of 44 young FH patients (sensitivity; 54.6%).
Conclusions: Both ATT measurement and DNA analysis are highly specific and sensitive for diagnosing FH patients. For young FH patients ATT measurement is not efficacious and DNA analysis is a prerequisite for identifying young FH patients.