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## Effect of a Pre-Designed Exercise Program and Metformin on Sub-clinical Atherosclerosis Among Individuals with Impaired Glucose Tolerance

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Pre-diabetes is associated with a high risk of atherosclerosis which can be detected by measuring sub-clinical atherosclerosis. We studied the effect of pre-designed exercise program or metformin on the progression of subclinical atherosclerosis among individuals with impaired glucose tolerance (IGT). One hundred and twenty people with IGT, determined by 75 g oral glucose tolerance test (OGTT) were recruited. They were allocated to four groups; pre-designed exercise (IGT-E), metformin 500mg once daily group (IGT-M), combined intervention group (IGT-EM), control group without any intervention (IGT-C), by block randomization method. Interventions were continued for six months, and carotid artery intima-media thickness (CIMT) was measured at the baseline, at the end of six months of intervention and at 18 months after an intervention-free period of one year. Mean(SD) age of IGT-C (n=30), IGT-E (n=30), IGT-M (n=30) and IGT-EM (n=30) at baseline were 43.9(8.7), 41.0(8.7), 50.6(8.2) and 48.8(8.4) years. The CIMT difference in right posterior wall at six months when compared to baseline in IGT-C, IGT-E, IGT-M and IGT-EM were [ $\{-0.004\text{mm}, (p=0.63)\}$ ,  $\{0.047\text{mm}, (p<0.001)\}$ ,  $\{0.034\text{mm}, (p<0.001)\}$  and  $\{0.046\text{mm}, (p<0.001)\}$ ] respectively. The CIMT difference in left posterior wall at six months when compared to baseline in IGT-C, IGT-E, IGT-M and IGT-EM were [ $\{-0.014\text{mm}, (p=0.23)\}$ ,  $\{0.051\text{mm}, (p<0.001)\}$ ,  $\{0.056\text{mm}, (p<0.001)\}$  and  $\{0.073\text{mm}, (p<0.001)\}$ ] respectively. The CIMT difference in right posterior wall at 18 months when compared to baseline in IGT-E, IGT-M and IGT-EM were [ $\{0.019\text{mm}, (p=0.004)\}$ ,  $\{0.016\text{mm}, (p=0.03)\}$  and  $\{0.046\text{mm}, (p<0.001)\}$ ] respectively. Further, the CIMT difference in left posterior wall at 18 months when compared to baseline in IGT-E, IGT-M and IGT-EM were [ $\{0.026\text{mm}, (p=0.004)\}$ ,  $\{0.029\text{mm}, (p<0.001)\}$  and  $\{0.048\text{mm}, (p<0.001)\}$ ] respectively. Significant reduction of posterior wall CIMTs was observed in all intervention groups at six months and at 18 months when compared to the baseline. But, right and left posterior wall CIMTs showed a significant increase [ $\{0.044\text{mm}, (p<0.001)\}$  and  $\{0.04\text{mm}, (p<0.001)\}$ ] in IGT-C during 18 months of follow-up. Pre-designed exercise program, metformin monotherapy or the combination of the two were effective in reducing the progression of sub-clinical atherosclerosis among individuals with impaired glucose tolerance.

*Keywords: Exercise, Impaired glucose tolerance, Metformin, Pre-diabetes, Sub-clinical atherosclerosis.*