**DOES CARDIORESPIRATORY FITNESS MODULATE THE INCIDENCE OF TYPE 2 DIABETES IN PATIENTS ON STATIN THERAPY**

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**Objective:** Several studies have reported a higher, dose-related risk for developing type 2 diabetes mellitus (T2DM) in those treated with statins compared to placebo or standard care. However, the benefit of statin treatment for prevention of CVD and all-cause mortality outweigh the risk, even among patients with existing T2DM and statin use is not likely to decline. Thus, lifestyle interventions, including adequate physical activity (PA) to improve cardiorespiratory fitness (CRF) have been proposed as ways to counter the risk of T2DM in statin-treated patients. However, the impact of increased CRF on the development of T2DM in statin-treated patients has not been examined. In addition, some studies suggest that improvements in CRF in response to exercise training may be blunted by statin therapy. Therefore, we sought to assess the impact of CRF on the incidence of T2DM in dyslipidemic patients treated with statins.

**Method:** Our participants (n=4,092; age=58.8±10.9 years), had no evidence of T2DM prior to statin therapy and had a normal exercise tolerance test performed during 1986 and 2014. We formed four fitness categories based on age and peak Metabolic Equivalents (MET) achieved: Least-fit (n=954); Low-fit (n=1,201); Moderate-fit (n=1,242); and High-fit (n=695). Dyslipidemic patients (n=3,001; age=57.2±11.2 years) not treated with statins and no evidence of T2DM prior to a normal exercise test served as controls.

**Results:** T2DM incidence was 24% higher in statin-treated compared to non-statin treated patients. In the statin-treated group, 1,075 (26.3%) developed T2DM with an average annual incidence rate of 30.6 events per 1,000 person-years. Incidence of T2DM declined by 6% per 1- MET increase in exercise capacity (hazard ratio [HR] 0.94; [95% confidence interval (CI) 0.91-0.97]). Compared to the Least-Fit, adjusted risk declined progressively with increasing fitness and was 34% lower for High-fit individuals (HR 0.66 [95% CI 0.53-0.82]).

**Conclusion:**Incidence of T2DM in dyslipidemic patients on statins was inversely and independently related to CRF. Improving CRF may modulate the potential diabetogenic effects of statins.