

Statins, Cardiorespiratory Fitness and Cardiometabolic Health



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Results of several clinical trials have shown that statin treatment substantially reduces morbidity and mortality of individuals with coronary heart disease and those with high risk of cardiovascular disease (CVD) who do not have coronary heart disease.

Data from large epidemiologic studies support an inverse, graded, independent, and robust association between cardiorespiratory fitness (CRF) and mortality risk in apparently healthy individuals and in patients with CVD. The risk is highest for patients within the lowest fitness category, with a progressive decline in risk observed as fitness increases irrespective of sex, presence of other risk factors, or age.

There is also evidence suggesting that statins may attenuate exercise capacity. To assess the potential CRF-Statin interaction, we examined the combined effects of CRF and statin treatment on all-cause mortality. We identified 10,043 dyslipidemic patients who had completed an exercise stress test and had no evidence of ischemia. We assigned them to one of four fitness categories based on peak metabolic equivalents (MET) achieved during the exercise test: Least-fit; Low-fit, Moderate-fit and High-fit and eight categories based on fitness status and statin treatment.

We found that both statin therapy and increased CRF lowered the mortality risk. However, the combination of statin treatment and increased CRF results in substantially lower mortality risk than either therapy alone, reinforcing the importance of physical activity for individuals with dyslipidaemia. We also observed similar findings in hypertensive, dyslipidemic patients treated with statins.

Recent studies have also 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 therefore, statin use is not likely to decline. Thus, lifestyle interventions, including improved CRF have been proposed as ways to counter the risk of T2DM in statin-treated patients.

Therefore, we assessed the CRF-Statin-T2DM association in a cohort of 4,092 dyslipidemic patients treated with statins (age=58.8±10.9 years), with no evidence of T2DM prior to statin therapy and a normal exercise response to a standardized exercise test. We assigned them to four fitness categories based on age and peak MET achieved: Least-fit; Low-fit; Moderate-fit; and High-fit. 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.

We found that the T2DM incidence was 24% higher in statin-treated compared to non-statin treated patients. When CRF was considered, T2DM incidence declined by 6% per 1-MET increase in exercise capacity. Compared to the Least-Fit, adjusted risk declined progressively with increasing CRF and was 34% lower in patients within the highest CRF category. Compared to the non-statin cohort, the incidence of T2DM risk was 50% higher in the Least-fit and 22% in the Low-fit individuals. The risk was not elevated in the Moderate-Fit and High-Fit patients.

Collectively, these findings support that statin treatment and increased CRF are independently associated with low mortality risk among dyslipidemic individuals. The combination of statin treatment and increased CRF can result in substantially lower mortality risk than either alone, reinforcing the importance of physical activity for individuals with dyslipidemia. In addition, increased CRF can attenuate the increased risk of statin-induced T2DM incidence.