Statins and the risk of pancreatic cancer in diabetic patients

Pancreatic cancer is the fourth leading cause of cancer deaths in the United States. Only approximately 15% to 20% of pancreatic cancer patients are diagnosed early enough to be eligible for surgery. The 1- and 5-year survival rates for all stages of pancreatic cancer combined are 20% and 6%, respectively. The low survival rate of patients with pancreatic cancer suggests a need for better treatment, early detection and improved chemoprevention strategies. Statins, which are inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase, are regarded as a first-line medical therapy for hypercholesterolemia. Several studies have implied that statins may exhibit chemopreventive potential for specific cancers; however, no convincing evidence that statins decrease the risk of pancreatic cancer has been reported.

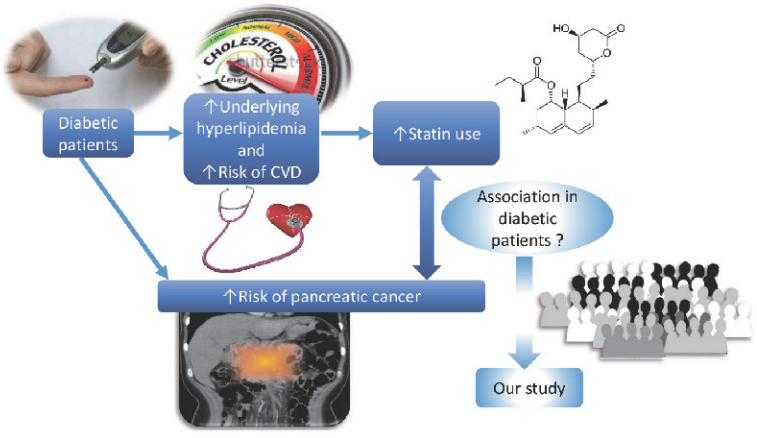

Figure 1. The concepts underlying our research motives.

Diabetic patients have a greater likelihood of underlying hyperlipidemia and cardiovascular disease, which has led to greater statin use among such patients than among nondiabetic subjects. Diabetic patients also tend to have a higher risk of developing pancreatic cancer. We conducted a retrospective study to assess the unconfirmed association between statin use and the risk of pancreatic cancer in chronic type 2 diabetic patients (Figure 1).

Our study used the National Health Insurance Research Database (NHIRD); from this database, a total of 1,140,617 patients with a first-time diagnosis of type 2 diabetes mellitus were selected based on ICD-9 (International Classification of Diseases, Ninth Revision) codes. In the diabetic cohort, 2,341 patients with newly diagnosed pancreatic cancer from 1999-2010 were identified. The percentage of pancreatic cancer cases in the diabetic cohort was 0.21%. The incidences of pancreatic cancer were 20.27 per 10^5 person-years in the statin user group and 43.75 per 10^5 person-years in the statin nonuser group. A Cox proportional hazards regression model with time-dependent covariates was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of pancreatic cancer associated with statin use in the diabetic cohort. One-year follow-up intervals were utilized to assess statin use. After adjusting for confounders, we determined that statin use significantly decreased the risk of pancreatic cancer (adjusted HRs: 0.78 for 28-83 cDDD (cumulative defined daily dose) per year; 0.48 for 84-180 cDDD per year; and 0.33 for >180 cDDD per year). Our study shows that patients with a longer duration of statin use may have a lower cumulative event rate for pancreatic cancer. Kaplan-Meier analysis of statin nonusers and subjects with 0-1 year, 1-2 years, 2-3 years and >3 years of statin use revealed a significant duration effect, with a log-rank p value <0.001 (Figure 2). A potential mechanism is that statins may decrease the risk of pancreatic cancer in diabetic patients by inhibiting mevalonic acid, IGF-1 and the IGF-1 receptor.

In conclusion, this study found that statin use may reduce the risk of pancreatic cancer in type 2 diabetic patients. The ability of statins to reduce pancreatic cancer risk may depend on the presence of diabetes. However, further research is needed to clarify this association.

References

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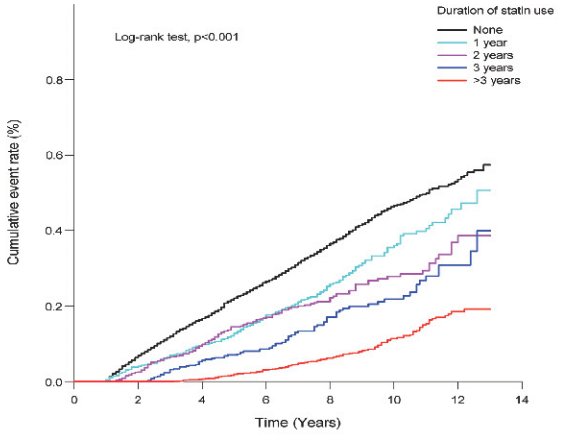

Figure 2. Cumulative rates of pancreatic cancer according to different durations of statin use during the follow-up period in the type 2 diabetes cohort.

Mediating analysis of the relationship between obesity and childhood asthma

Obesity and asthma are two significant public health problems with increasing prevalence during childhood. Prospective studies have suggested that obesity precedes the development of asthma. Several possible mechanisms have been postulated to explain this relationship, including an obesity-related reduction in lung volume, inflammatory mediators, obesity-related changes in hormone levels, and dyslipidemia. Based on our baseline Taiwan Children Health Study (TCHS) cohorts, we performed prospective follow-up evaluations using parent and child questionnaires, obesity measures, physical fitness levels, and pulmonary function tests.

We applied a novel approach to investigate the pathogenic mechanisms. Using the structural equation model (SEM), we successfully constructed models of the relationships between obesity and physical fitness, sedentary time, and childhood asthma. The SEM, first used in social science research during the 1980s, is a type of polybasic statistical model that combines factor analysis and pathway analysis and can be used with different types of variables and hierarchical data structures for causal inference. By applying the SEM to our TCHS dataset, we found that low physical fitness and high sedentary time were the leading factors associated with central obesity in children and subsequent asthma development. We also applied the widely used generalized estimating equation and conducted the survival analysis of longitudinal data in three-year measurements, and the results were consistent with the conclusion that low phys-