Risk of Diabetes Mellitus after First-attack Acute Pancreatitis: A National Population-based Study

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Introduction
A recent meta-analysis of 24 prospective studies on patients with first-episode acute pancreatitis (AP) shows that DM develops in 15% within one year and the risk at least doubles over five years after AP (relative risk 2.7, 95% confidence interval [CI] 1.9-3.8). Without a population-based control, the question of whether and to what extent AP increases the risk of DM remains to be answered.

Methods
Database
Data in this study were retrieved from Taiwan National Health Insurance Research Database (NHIRD). The study cohort was drawn from a subset of the NHIRD, the National Health Insurance Database of 2000 (LHID-2000). The LHID-2000 included one million randomly selected beneficiaries, which represented about 10% of the Taiwanese population enrolled in 2000.

Definitions and study cohort
AP was defined by ICD-9-CM code 577.0 in any position of the five diagnoses from the inpatient claims data.

Figure 1 shows the process of patient enrollment.

End-point
We identified the first outpatient or inpatient diagnosis for DM (including ICD-9-CM codes 250, 251.3 (post-hypoglycemia) and 251.8 (other specified disorders of pancreatic internal secretion)) between the index dates in 2000 and the last day of 2010 as the study end-point. All the study subjects were followed from the index date to occurrence of end-point, withdrawal from the insurance system, or December 31, 2010, whichever date came first. Subjects with the last two conditions were considered censored in the analysis.

Statistical analysis
Cox proportional hazard regression models were performed with adjustment for age, sex, income level, geographic area, urbanization, and the Charlson index (continuous variable) to estimate the hazard ratio (HR) of DM in relation to AP. Because both severity and recurrence of AP are associated with increased risk of DM, we repeated the analyses according to the severity and by excluding patients with recurrence (before the diagnosis of DM) after the first-attack (n=823, 27.7%). Finally, we also assessed the risk of DM requiring long-term insulin therapy (ICD codes 250.1 and 250.8) after mild AP. A two-tailed P value <0.05 was considered statistically significant.

Results
The overall age- and sex-specific IDs and relative hazards of DM in both groups are shown in Table 2. Kaplan-Meier failure estimates of DM between the two groups are shown in Figure 2. Stratified analyses by severity of AP are shown in Tables 3 and 4. The exclusion of subsequent recurrence of AP only slightly reduced the HRs, but did not change the results (data not shown).

As the endpoint was limited to DM requiring long-term insulin therapy, the overall adjusted RR was 5.05 (95% CI 1.75-14.55) in patients with mild AP. Due to small number of the outcome (n=90), age- and sex-specific analyses were not performed.

Conclusions
This is the first population-based study to demonstrate a two-fold increase of DM after first-attack AP. Results of this study would provide valuable information for physicians and patients on the need and guidance of long-term follow-up for the development of DM after first-time AP attack.