RESPONSE TO COMMENT ON CHO ET AL.

Antidiabetic Medications and Mortality Risk in Individuals With Pancreatic Cancer–Related Diabetes and Postpancreatitis Diabetes: A Nationwide Cohort Study. Diabetes Care 2019;42:1675–1683

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We thank Devouge et al. (1) for their interest in our nationwide cohort study that will contribute meaningfully to the changing field of diabetes of the exocrine pancreas. The authors made a comment about the possibility of including individuals with undetected type 2 diabetes in the cohort of postpancreatitis diabetes mellitus (PPDM) we established (2). The issue of undetected type 2 diabetes is common and ubiquitous. This is because of suboptimal screening for diabetes in general and PPDM in particular. To ensure that this perennial issue does not cripple accuracy of data in the context of pancreatitis, the use of two terms (as appropriate) is advocated: "new-onset diabetes after pancreatitis" (NODAP) and PPDM (3,4). When an individual is confirmed not to have preexisting diabetes based on HbA_{1c} level at the first episode of pancreatitis, the term NODAP is used. The term PPDM is reserved for the occurrence of diabetes after the first episode of pancreatitis in individuals with no known evidence of prior diabetes, irrespective of baseline HbA_{1c} level. Given that data on HbA_{1c} were not available in our epidemiological study, we used the term PPDM. A prospective clinical longitudinal cohort study from our research group is in the pipeline to investigate the incidence and risk factors for NODAP, and that study includes baseline and regular follow-up HbA_{1c} and fasting plasma glucose data.

The authors of the comment also speculated that the survival benefit of metformin might be limited to individuals with postacute pancreatitis diabetes mellitus (PPDM-A), and not those with postchronic pancreatitis diabetes mellitus (PPDM-C) because of possible excess adiposity of the former (resulting in higher effectiveness of metformin). Given that the 2019 MRI study of individuals after acute pancreatitis by our group showed the importance of visceral and ectopic fat (specifically, intrapancreatic fat deposition) in the pathogenesis of diabetes in this study population (5), we certainly agree that excess adiposity could act as an effect modifier of the association between the use of metformin and mortality in individuals following pancreatitis. Unfortunately, we did not have data related to adiposity in our nationwide epidemiological study. It is worth mentioning, though, that the proportion of metformin ever-users was 60.8% (n = 377 of 620) and 56.0% (n = 121 of 216) among individuals with PPDM-A and those with PPDM-C, respectively. The ever-use of metformin was associated with a 51% reduction in mortality risk in individuals with PPDM-A and a 37% reduction in those with PPDM-C. This difference was not statistically significant (P for interaction = 0.53).

In addition, Devouge et al. (1) interpreted the relatively low mean dose of metformin (1,000 mg/day) in our study as poor tolerance in individuals with PPDM-C. It is important to clarify that the dose was based on the first prescription fill in new users of metformin, and the average first-prescribed dose of metformin was 1,000 mg/day in both individuals with PPDM-A and those with PPDM-C. The relatively low mean dose of metformin might have been related to the common practice of starting with a low dose of metformin and there might have been no need to increase the dose substantially during the study period because of the effectiveness of metformin in reducing blood glucose levels in PPDM-C.

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