

Prevalence and Risk Factors of Gastroesophageal Reflux Disease in Patients with Type 2 Diabetes Mellitus (*Diabetes Metab J* 2016;40:297-307)

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Gastroesophageal reflux disease (GERD) is common in patients with type 2 diabetes mellitus (T2DM), and the manifestations of GERD in diabetic patients may be more atypical than those of the general population [1,2]. A recent meta-analysis of nine studies involving 9,067 cases and 81,968 controls identified a significant association between diabetes and the risk of GERD (overall odds ratio, 1.61; 95% confidence interval, 1.36 to 1.91; $P=0.003$) [3]. Risk factors for GERD in diabetes include autonomic neuropathy, elevated body mass index (BMI), longer duration of diabetes and poor glycemic control [4]. However, further studies should be undertaken to clarify the pathophysiologic mechanism of GERD in patients with T2DM.

In this article entitled “Prevalence and risk factors of gastroesophageal reflux disease in patients with type 2 diabetes mellitus,” Ha et al. [5] evaluated the prevalence and risk factors (including autonomic neuropathy) of GERD in patients with T2DM. Interestingly, the prevalence of GERD in patients with T2DM showed no difference from that of controls, which is contrary to the conclusion of the recent meta-analysis by Sun et al. [3]. Furthermore, GERD was not associated with peripheral and cardiovascular autonomic neuropathy, age, or duration of diabetes in patients with T2DM. There are several issues that need to be addressed.

First, there is a possibility that the prevalence of GERD may

have been under- or overestimated in the present study. The diagnosis of GERD and its related clinical symptoms is challenging. GERD includes erosive esophagitis and non-erosive reflux disease, and one of the reasons for the difficulty in identifying causative factors for GERD is the confusion between reflux esophagitis and non-erosive reflux disease [6]. Lluch et al. [1] reported the prevalence of asymptomatic GERD confirmed by pH study, which was significantly higher in diabetic patients than in healthy controls. Esophageal pH monitoring and manometry are the gold standards for diagnosis of GERD and esophageal dysmotility [4]. Therefore, application of pH study and manometry in the present study could possibly alter the prevalence of GERD.

Second, a number of mechanisms have been proposed to elucidate the connection between diabetes and GERD. They include the effects of acute and long-term hyperglycemia on neuronal function and gastrointestinal motility, which result in esophageal dysmotility and gastroparesis. Patients with T2DM are often obese, predisposing them to GERD. Furthermore, hormonal changes such as decreased ghrelin and motilin levels occurring in obese diabetic patients have revealed associations with gastrointestinal dysfunction that may contribute to the development of GERD. And the use of diabetes medications such as metformin or glucagon-like peptide-1 receptor agonist is associated with an increased risk of symptomatic GERD in

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patients with T2DM [7]. In the present study, although the mean age of patients with T2DM was higher (57.7 ± 0.6 years vs. 52.7 ± 0.6 years, $P < 0.001$), BMI was higher (25.1 ± 0.2 vs. 23.4 ± 0.2 , $P < 0.001$) and cigarette use was more frequent (24% vs. 11%, $P = 0.008$) compared with control group, the prevalence of GERD and GERD symptoms in patients with T2DM showed no difference from that of controls. These results are incompatible with the aforementioned report [3], but the possible reasons for these results were not discussed in the study.

Finally, there are several interesting reports about proton pump inhibitor (PPI) therapies in diabetic patients. Hershcovici et al. [8] found that T2DM patients with GERD are more likely to fail PPI therapies compared with healthy controls. Because failure rates of PPIs in diabetic patients was higher in obese patients, it appears to be dependent on BMI. However, PPIs may exhibit a beneficial effect in the treatment of diabetes as well as GERD. A retrospective study revealed a significant decrease in glycosylated hemoglobin of 0.6% in non-insulin-using T2DM patients [9]. Furthermore, a recent randomized clinical trial reported that PPIs improve glycemic control, suggesting additional benefits of PPIs in diabetic patients with GERD [10].

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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