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Incidence of Esophageal Adenocarcinoma Among Symptomatic Reflux Patients Without Erosive Disease on Endoscopy is Similar to the General Population

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Holmberg D, Santoni G, von Euler-Chelpin M, et al. Non-erosive gastro-oesophageal reflux disease and incidence of oesophageal adenocarcinoma in three Nordic countries: population based cohort study. *BMJ* 2023;382.

Chronic gastro-esophageal reflux disease (GERD) symptoms (eg, heartburn and regurgitation) are a common indication for esophagogastroduodenoscopy (EGD) to screen for Barrett’s esophagus among other pathologies. In the absence of warning signs or symptoms, the vast majority of patients will not have erosive reflux findings such as esophagitis, peptic stricture, or Barrett’s esophagus. Although erosive reflux disease is associated with esophageal adenocarcinoma (EAC), the association between nonerosive GERD symptoms and EAC is not well established.

In this population-based cohort study conducted across 3 Nordic countries (Denmark, Finland, and Sweden), health care registry data from 1987 to 2019 were analyzed to examine incidence of EAC. Patients with GERD who underwent at least 1 EGD were included, and

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2 cohorts were examined. First was the non-erosive GERD cohort, patients with normal findings on the first EGD (defined as absence of erosive esophagitis or other esophageal diagnosis 12 months after the time of the first EGD). The second was the validation erosive GERD cohort, patients with a diagnosis of erosive GERD.

Overall, 285,811 patients were in the non-erosive GERD cohort, comprising 2,081,051 person-years. Among the non-erosive GERD cohort, 0.08% developed EAC with an incidence rate of 11.0 cases per 100,000 person-years. Compared with that reported for the general population, the overall standardized incidence ratio of EAC was 1.05 (95% confidence interval 0.91–1.18). The incidence ratio did not increase with longer follow-up of 15 to 31 years.

On the other hand, in the 200,745 patients in the erosive GERD validation cohort (1,750,249 person-years) 0.27% developed EAC with an incidence rate of EAC of 31 cases per 100,000 person-years. The standardized incidence ratio of EAC was 2.36, and point estimates increased and became more pronounced with longer follow-up.

Thus, in this study, the incidence of EAC among symptomatic patients with non-erosive findings on endoscopy was similar to that of the general population and did not increase over time, whereas the incidence of EAC was higher and increased over time among patients with erosive reflux disease, as was expected. This is a well designed population-based study with several strengths, including a large sample size, long follow-up duration, robust and validated health registry data, and validation against a cohort of erosive GERD. At the same time, population-based cohort studies are vulnerable to risks such as detection bias. Furthermore, in this study, the standardized incidence ratios were based on comparisons to the incidence of EAC in the general Nordic populations across the national cancer registries. It is important to note that the patients with non-erosive GERD were patients with reflux symptoms but were not necessarily confirmed with objective GERD based on reflux monitoring, and therefore the group likely included patients with functional disease. As such, these results cannot be extrapolated to a pathologic GERD patient population. Nonetheless, the data are intriguing and underscore current clinical practice, which is to not repeat endoscopy for screening purposes in patients with reflux symptoms and absence of erosive disease on endoscopy.

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