

Gastroesophageal reflux as a precursor to malignancy of the nasopharynx and paranasal sinuses in the United States



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Abstract

Introduction: Chronic inflammatory states have been linked to the development of malignancy. Gastroesophageal reflux disease (GERD) is a known risk factor for esophageal adenocarcinoma as the end result of chronic inflammatory changes. Our purpose was to investigate the impact of GERD on the risk of malignancy in the nasopharynx and paranasal sinuses. **Methods:** The Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database was queried as a case-control study of United States adults aged 65 years and older from 2003 to 2011. The study cohort included patients diagnosed with malignancy of the nasopharynx and paranasal sinuses. GERD was examined as an exposure. Multivariable unconditional logistic regression was calculated. **Results:** A total of 2,001 patients with malignancy of the nasopharynx or paranasal sinus were compared with 2,001 non-diseased patients matched for gender, age, race, geography, and year of diagnosis. GERD was associated with a greater odds of developing malignancy of the nasopharynx (aOR 1.694; 95% CI 1.293, 2.218) and paranasal sinuses (aOR 1.511, 95% CI 1.218, 1.876). **Conclusions:** GERD is associated with the presence of malignancy of the nasopharynx and paranasal sinuses in the United States elderly population.

Results

A total of 4,002 patients were included from the SEER-Medicare linked database query. 2,001 patients had a diagnosis of carcinoma of the nasopharynx or paranasal sinus and were included in the case group for analysis. Of these patients, there were 755 nasopharyngeal and 1,246 paranasal sinus malignancies. 2,001 control patients were matched for gender, age of diagnosis, year of diagnosis, race, geography, and urban versus metropolitan environment. Overall, there were 2,374 males (60.32%) and 1,628 females (40.68%).

GERD was associated with a greater odds of developing malignancy of the nasopharynx (aOR 1.694; 95% CI 1.293, 2.218) and paranasal sinuses (aOR 1.511, 95% CI 1.218, 1.876). Each of these calculations reached statistical significance (Table 1).

The prevalence of malignancy in the non-exposed and exposed populations is reported in Table 2. The relative risk of nasopharynx malignancy was 2.45 times greater in subjects with GERD compared to controls (95% CI 2.29-2.61), while the relative risk of paranasal sinus malignancy was 2.27 times greater in patients with GERD.

Table 2. Prevalence, relative risk, attributable risk, and number needed to harm for malignancies of the nasopharynx and paranasal sinus.

	Prevalence with GERD (%)	Prevalence without GERD (%)	RR	95% CI	AR	NNH
Nasopharynx	0.052	0.021	2.45	2.29-2.61	0.000306	3264
Paranasal Sinus	0.081	0.036	2.27	2.14-2.39	0.000452	2213

Gastroesophageal reflux disease, GERD. Relative risk, RR. Confidence interval, CI. Attributable risk, AR. Number needed to harm, NNH.

Introduction

GERD has a significant association with the development of esophageal adenocarcinoma.¹⁻³ The natural history of this disease is likely due to chronic inflammation of the esophageal mucosa that results in cellular transformation.^{4,5} Other inflammatory conditions are linked to the development of malignancy such as ulcerative colitis, hepatitis, and sinonasal tract inflammatory diseases like chronic rhinosinusitis and allergic rhinitis.

Malignancies of nasopharynx and paranasal sinuses account for more than 40,000 cases of cancer globally each year. The etiology of these malignancies is thought to be multifactorial and include alcohol and tobacco use, viral infections, environmental exposures, and chronic inflammatory conditions.

To date, there have been no studies examining the link between GERD and the development of malignancy in the nasopharynx and paranasal sinuses in the United States. Defining an association between GERD and malignancy of these sites may contribute to the understanding of inflammatory disease as a risk factor for cancer and aid in surveillance.

Methods and Materials

A case-control study was performed using the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database for adults in the United States aged 65 years and greater from 2003 to 2011. The study cohort included patients diagnosed with malignancy of the nasopharynx and paranasal sinuses. GERD was examined as an exposure. Controls were selected from a 5% random sample of Medicare beneficiaries without cancer. The cases and controls were matched according to gender, age group (66-69, 70-74, 75-79, 80-84, 85-99 years) and diagnosis years (calendar year was used for the control group) using propensity score matching. Multivariable unconditional logistic regression was calculated.

Table 1. GERD association with malignancy of the nasopharynx and paranasal sinus.

		No GERD (%)	GERD (%)	Odds Ratio (95% CI)	
				Unadjusted	Adjusted*
Nasopharynx	Control	630 (83.44)	125 (16.55)	1.545 (1.389, 1.902)	1.694 (1.293, 2.218)
	Case	536 (70.99)	219 (29.01)		
PSM	Control	955 (79.86)	251 (20.14)	1.499 (1.12, 2.013)	1.511 (1.218, 1.876)
	Case	904 (72.55)	342 (27.44)		

Gastroesophageal reflux disease, GERD. Confidence interval, CI. Paranasal sinus malignancy, PSM.

Discussion

This longitudinal population-based study is the first to examine the association between GERD and the development of nasopharyngeal and paranasal sinus malignancies in an elderly U.S. population. There is a significant association between GERD and the presence of malignancy at these subsites. Chronic inflammation has been described as an etiology for malignancies of the esophagus¹⁰, stomach, liver, and colon, and cellular mechanisms have been described for these processes.⁴ Presumably, an analogous mechanism may be operative in the nasopharynx and paranasal sinuses, and would have implications for understanding the role of chronic inflammation in these cancers. Regardless of causality, or lack thereof, the systematic nature of the association in this large, population-based study may be relevant for identifying an at-risk population, improving surveillance, and initiating earlier treatment.

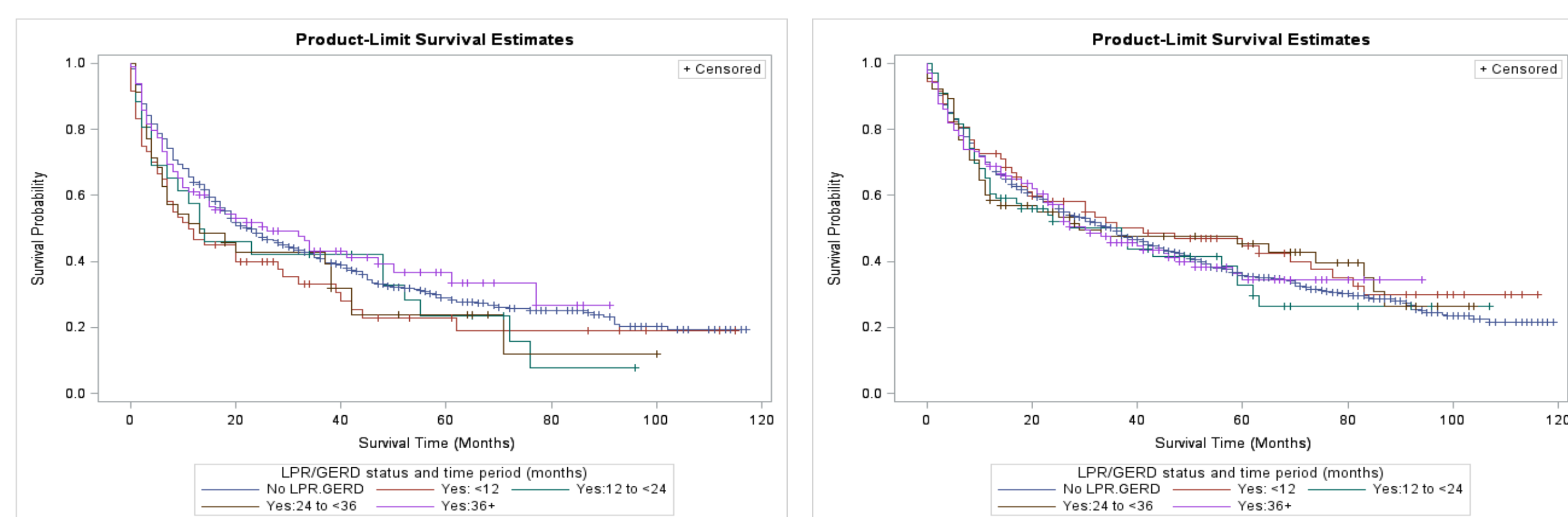


Figure 1. (Left) Kaplan-Meier survival curves by GERD exposure status of the nasopharynx. (Right) Kaplan-Meier survival curves by GERD exposure status of the paranasal sinus.

Conclusions

GERD is associated with the development of malignancy of the nasopharynx and paranasal sinuses in an elderly U.S. population. The increased relative risk for these cancers in the elderly population suggests an opportunity for earlier detection and intervention. Future studies are necessary to determine this effect on a younger cohort and to establish causation.

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