The Epidemiology of Immune Checkpoint-Inhibitor-Induced Esophagitis: A Population-Based Study

Khaled Alsabbagh Alchirazi, Ahmed Eltelbany, Abdul Mohamed, Madhusudhan Sanaka, Prashanthi Thota.

Cleveland Clinic Foundation

Introduction

- Immune checkpoint inhibitor (ICI) induced esophagitis is increasingly recognized as a severe adverse event of ICIs.
- There are limited epidemiological studies with small sample sizes.
- We aim to utilize a large database to investigate the epidemiology of ICI-induced esophagitis and describe underlying associations.

Methods

- A multi-institutional database (Explorys Inc, Cleveland, OH, USA), an aggregate of electronic health record data from 26 US healthcare systems, was surveyed.
- A cohort of patients on ICIs (nivolumab, pembrolizumab, ipilimumab and atezolizumab) was identified from 2011 to 2022.
- Subsequently, patients who developed Systematized Nomenclature of Medicine-Clinical Terms diagnosis of esophagitis taking ICIs were selected.
- The prevalence of ICI-induced esophagitis was calculated, and underlying associations were described.

Results

- Of the 70,383,890 patients in the database, we identified 20,200 (0.03%) with a history of ICI use. There were 2430 (12%) patients who developed a new diagnosis of ICI-induced esophagitis at least 1 day of starting ICI therapy. Patients who developed ICI-induced esophagitis were more likely to be Caucasian [OR: 1.32; 95% CI 1.17–1.50] and older than 65 years [OR: 1.14; 95% CI 1.05–1.25]. There was no statistically significant gender-based differences. When compared to patients on ICI therapy who did not develop esophagitis, patients with ICI-induced esophagitis were more likely to have a history of tobacco use [OR: 1.59; 95% CI 1.46–1.74], history of alcohol use [OR: 1.55; 95% CI 1.34–1.81] and obesity [OR: 1.49; 95% CI 1.36–1.64] (figure 1). Patients who received Nivolumab [OR: 8.43; 95% CI 7.83–9.07, p< 0.0001], pembrolizumab [OR: 7.97; 95% CI 7.48–8.48, p< 0.0001], ipilimumab [OR: 4.52; 95% CI 3.27–6.23, p= 0.0007] and atezolizumab [OR: 7.92; 95% CI 6.88–9.11, p< 0.0001] had high odds of developing ICI-induced esophagitis (Figure2).

	ICI+Esophagitis (n=2,430)	ICI-Esohagitis (n=17,770)	OR (CI)	p-value
Age				
18-65	840 (34%)	6,650 (37%)	0.88 (0.81-0.97)	0.0063
>65	1,610 (66%)	11,230 (63%)	1.14 (1.05-1.25)	0.0033
Sex				
Female	1,040 (43%)	7,530 (42%)	1.02 (0.93-1.11)	0.6919
Male	1,390 (57%)	10,250 (58%)	0.98 (0.90-1.07)	0.6535
Race				
Caucasian	2,110 (87%)	14,800 (83%)	1.32 (1.17-1.50)	< 0.0001
Non-Caucasian	320 (13%)	2,970 (17%)	0.76 (0.67-0.86)	< 0.0001
Esophagitis Risk Factors				
Alcohol abuse	220 (9%)	1,070 (6%)	1.55 (1.34-1.81)	< 0.0001
Smoking history	940 (39%)	5,040 (28%)	1.59 (1.46 -1.74)	< 0.0001
Obesity	750 (31%)	4,090 (23%)	1.49 (1.36-1.64)	< 0.0001

Table 1: Baseline characteristics of patients receiving immune checkpoint-inhibitors. Univariate analysis used to calculate OR. OR; odds ratio, CI; confidence interval, ICI; immune checkpoint-inhibitors.

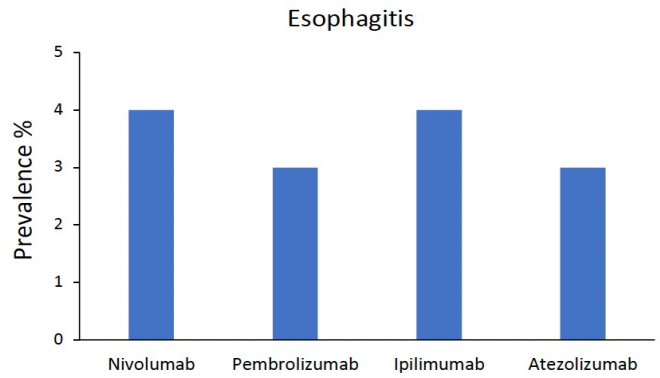

Figure 1: Prevalence of selected immune checkpoint-inhibitors demonstrating the risk of immune checkpoint-inhibitors induced esophagitis .

Discussion

This is the largest study evaluating the epidemiology of ICI-induced esophagitis, confirming an increase in esophagitis risk. Patients with ICI-induced esophagitis were more likely to be Caucasian, older than 65, with a history of tobacco and alcohol use, and obese. The risk of esophagitis should be discussed with patients before initiating these agents, and close follow-up with gastroenterologists is needed.