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Characteristics of early- versus late-onset esophageal adenocarcinoma: insights from the National Inpatient Sample 2016-2020

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Abstract

Background The incidence of early-onset esophageal adenocarcinoma (EAC) in adults aged <50 years is rising, yet remains under-investigated. This study compared demographic, clinical and socioeconomic predictors of early- vs. late-onset EAC using national hospitalization data.

Methods We analyzed adult patients diagnosed with EAC from the National Inpatient Sample (2016-2020). Cases were stratified into early-onset (age <50 years) and late-onset (≥50 years), and further categorized by tumor location (upper, middle, lower esophagus). ICD-10-CM codes were used to identify diagnoses. Demographics, comorbidities and socioeconomic variables were compared using Rao-Scott chi-square tests.

Results Among 105,228 EAC admissions, early-onset cases comprised 5.89%. Lower esophagus involvement was most common (74.6%). Compared to late-onset patients, early-onset cases had a lower proportion of Caucasians (71.5% vs. 79.8%, P<0.001) and higher proportions of Black (13.9% vs. 9.6%) and Hispanic individuals (7.0% vs. 5.4%). Smoking (25.1% vs. 17.9%), obesity (11.4% vs. 8.4%), and drug use (28.9% vs. 19.7%) were more prevalent in early-onset patients (P<0.001). In contrast, late-onset patients had higher rates of hypertension (47.1% vs. 26.7%), diabetes, chronic obstructive pulmonary disease and gastroesophageal reflex disease (P<0.001). Early-onset patients were less likely to be insured with Medicare (6.8% vs. 57.9%), and more likely with Medicaid (35.0% vs. 10.6%) or to be self-payers (3.9% vs. 1.8%).

Conclusions Early-onset EAC presents with distinct racial, socioeconomic and clinical profiles compared to late-onset disease. These findings underscore the need for tailored screening strategies and further research to address disparities and risk factors in younger populations.

Keywords Esophageal adenocarcinoma, early-onset, late-onset, National Inpatient Sample, risk factors

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Introduction

Esophageal adenocarcinoma (EAC) is a gastrointestinal cancer with a rapidly rising incidence and poor overall prognosis, accounting for approximately 0.6 million new cases and 0.54 million deaths worldwide in 2020 [1]. It is the eleventh most diagnosed cancer, and the seventh leading cause of cancer-related deaths globally [2]. Several risk factors for esophageal cancer have been extensively studied, including advanced age (>50 years), tobacco smoking, alcohol use, and gastroesophageal reflux disease (GERD) with esophagitis [3]. The median age at EAC diagnosis is 60 years [4].

Since advanced age is a well-recognized strong risk factor, screening modalities and endoscopy for diagnosing EAC are primarily employed in individuals older than 50 years, resulting in significantly fewer endoscopies in younger patients compared to those aged >50 years [5]. As EAC is relatively uncommon before age 50, data on the incidence, stage distribution and outcomes for this subgroup of EAC patients are relatively limited [4]. However, emerging studies have reported an increasing number of advanced-stage presentations in EAC patients younger than 50 years [6]. Subsequent studies have supported these findings, also indicating an increasing trend in the proportion of advanced disease among younger patients over decades, along with disproportionately poorer 5-year EAC-free survival and overall survival compared to older cohorts [4,7].

Given these trends, we hypothesized that early-onset EAC presents with distinct clinical characteristics compared to late-onset EAC. To test this, we aimed to analyze the characteristics and impact of specific predictors of early-onset EAC using the National Inpatient Sample (NIS) database from 2016-2020. We compared these findings to late-onset EAC, stratified by anatomical location.

Materials and methods

Database

NIS is the largest publicly accessible all-payer database for inpatient healthcare in the United States. It is a valuable resource for large-scale data analysis, providing regional and national insights into hospital utilization, access to care, costs, quality and outcomes. Developed as part of the Healthcare Cost and Utilization Project, the NIS is supported by a collaborative effort among federal and state agencies and the private sector under the guidance of the Agency for Healthcare Research and Quality. The database includes raw data from approximately 7 million hospital stays annually. Using discharge weights, researchers can extrapolate this data to represent about 35 million hospitalizations annually.

Study design

This research employed a retrospective case–control study design to evaluate the influence of specific predictors in early-onset EAC compared to late-onset EAC. Data from the NIS spanning the years 2016-2020 were used for the analysis.

Study population

The study population included adults (aged >18 years) hospitalized with a primary or secondary diagnosis of EAC. These cases were identified using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes. Gastroesophageal-junctional tumors, including Siewert III, were not included.

Study variables

Within the cohort of EAC hospitalizations, predictors such as patients' demographics, comorbidities, region, hospital type, insurance type, and median household income were analyzed. These variables were compared between early-onset and late-onset EAC within each anatomic location subtype. This includes upper-EAC (upper third of the esophagus), mid-EAC (middle third of the esophagus), and lower-EAC (lower third of the esophagus). Staging data could not be included in this study because of the limitations of the NIS dataset.

Definitions

In our study using the NIS database, the following variables were defined based on standardized diagnostic codes. As identified through clinical diagnosis, "GERD with esophagitis" refers to GERD accompanied by inflammation of the esophageal lining. "Obesity" is documented based on body mass index criteria or a clinical diagnosis indicating excessive body weight. "Hypertension, complicated" includes cases of high blood pressure with associated end-organ damage, such as heart failure or kidney disease. "Hypertension, uncomplicated" refers to high blood pressure without evidence of organ damage. "Diabetes with chronic complications" includes patients with diabetes mellitus who have long-term complications such as nephropathy, retinopathy or neuropathy. "Diabetes without chronic complications" refers to individuals with diabetes mellitus who do not exhibit significant long-term organ damage. "Peripheral vascular disease" includes conditions affecting blood circulation outside the heart and brain, such as arterial occlusive disease. "Chronic pulmonary disease" encompasses conditions such as chronic obstructive pulmonary disease (COPD), emphysema or chronic bronchitis, characterized by persistent respiratory impairment. "Smoking status" refers to patients with a documented history of tobacco use, including current and former smokers, as identified in the database. "Alcohol use" captures individuals with a history of alcohol consumption or dependence, as reported in their medical records. "Drug use" includes illicit drug use, dependence or

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abuse, based on diagnostic codes. "Household income" is categorized into quartiles, based on the median income for the patient's residential ZIP code, reflecting socioeconomic status. "Hospital region" is classified into 4 geographic areas, Northeast, Midwest, South and West, as defined by the US Census Bureau. "Primary insurance" is categorized into Medicare (federal insurance for individuals aged 65 and older or those with certain disabilities), Medicaid (state and federally funded insurance for low-income individuals), private insurance (coverage through employer-based or individually purchased plans), and self-pay, indicating uninsured patients responsible for their own medical expenses.

Statistical analysis

Analyses were performed using STATA/MP 17.0 software. Categorical variables were assessed using chi-square tests, while continuous variables were analyzed with *t*-tests. A P-value of <0.05 was considered statistically significant. Given the nature of the administrative data, a multivariate analysis was not conducted, and data related to cancer staging were not available.

Results

Early- vs. late-onset esophageal cancer (all segments combined)

A total of 105,228 hospitalizations for esophageal cancer were identified across all esophageal segments, with 5.89% categorized as early-onset and 94.11% as late-onset cases.

The racial distribution revealed that Caucasian individuals comprised the majority in both groups; however, the early-onset group had a significantly lower proportion of Caucasian patients (71.5% vs. 79.8%) and higher proportions of African American, Hispanic, Asian or Pacific Islander, Native American and other racial groups (all P<0.001).

Insurance patterns varied notably between groups. Medicare was the predominant payer among late-onset patients, while early-onset patients were more frequently covered by Medicaid or private insurance, or were self-pay (all P<0.001).

In terms of lifestyle factors, smoking (25.1% vs. 17.9%), alcohol use (8.6% vs. 7.3%), and drug abuse (28.9% vs. 19.7%) were significantly more common among early-onset patients compared to late-onset counterparts (all P<0.001). Conversely, late-onset patients had significantly higher rates of multiple comorbidities, including hypertension (complicated and uncomplicated), diabetes (with and without complications), chronic pulmonary disease and peripheral vascular disease (all P<0.001).

Notably, early-onset patients had a higher prevalence of obesity (11.4% vs. 8.4%; P<0.001), while GERD with esophagitis was slightly more common in the late-onset group (2.9% vs. 2.4%; P=0.02).

Socioeconomic distribution differed modestly: a greater proportion of early-onset patients were in the second income quartile (29.7% vs. 27.0%; P<0.001), and fewer were in the highest income quartile (17.5% vs. 21.5%; P<0.001). There were no statistically significant differences in geographic hospital region between the groups.

Table 1 summarizes the baseline characteristics of early- vs. late-onset esophageal cancer across all esophageal segments.

Early- vs. late-onset upper EAC

We identified 9190 hospitalizations for EAC involving the upper third of the esophagus. Among these, 6.36% of hospitalizations were categorized as early-onset EAC, while 93.63% were late-onset EAC.

The racial distribution showed that the majority of EAC cases, regardless of the age of onset, occurred among Caucasian individuals. However, a lower Caucasian percentage was noted in the early-onset upper EAC group (48.7% vs. 64.1%). Conversely, early-onset EAC had higher rates of all other racial groups, with a significant difference in racial distribution (P=0.03).

Regarding insurance utilization, there was a significant difference in primary insurance (P<0.001). Medicare was predominantly used by late-onset EAC patients. In contrast, among hospitalizations for upper EAC, early-onset cases were more likely to involve self-pay, private insurance or Medicaid.

Lifestyle factors also differed significantly between the groups. Smoking and illicit drug use were significantly more prevalent among early-onset EAC patients compared to their late-onset counterparts (35.1% vs. 21.2%; P=0.01, and 36.8% vs. 22.4%; P=0.009, respectively). Conversely, comorbid conditions such as COPD and hypertension (both complicated and uncomplicated) were more common in late-onset EAC patients.

No statistically significant differences were observed between early- and late-onset EAC groups in the prevalence of diabetes mellitus, GERD with esophagitis or obesity. Table 2 shows the baseline characteristics of patients with early- vs. late-onset EAC of the upper third of the esophagus.

Early- vs. late-onset middle EAC

We identified 17,569 hospitalizations for middle EAC, of which 5.06% were early-onset cases, and 94.9% were late-onset cases.

The majority of patients across both groups were Caucasian, followed by Black and Hispanic individuals. Early-onset EAC had a lower proportion of Caucasian and Hispanic patients and a higher proportion of Black patients compared to late-onset EAC. There was a significant difference in racial distribution (P<0.001).

In terms of insurance coverage, early-onset patients were more likely to use Medicaid, self-pay or private insurance, while late-onset cases predominantly relied on Medicare.

Table 1 Baseline demographics and comorbidities of patients who were diagnosed with early- vs. late-onset esophageal cancer across all segments

Variables	Total esophageal cancer	Subdivisions based on age of onset		
		Early-onset	Late-onset	P-value
No. of patients; N (%)	105,228 (100%)	6194 (5.89%)	99,034 (94.11%)	
Age (mean years ±SD)	66.5±0.34	43.59±0.61	67.99±8.90	<0.001
Female sex, (%)	21.74	19.74	21.86	<0.001
Race (%)				
Caucasian	79.3	71.5	79.8	<0.001
African American	9.8	13.9	9.6	<0.001
Hispanic	5.5	7.0	5.4	<0.001
Asian or Pacific Islander	2.4	3.5	2.3	<0.001
Native American	0.47	0.84	0.44	<0.001
Others	2.5	3.3	2.4	<0.001
Comorbidities (%)				
Smoking	18.3	25.1	17.9	<0.001
Alcohol use	7.4	8.6	7.3	<0.001
GERD with esophagitis	2.8	2.4	2.9	0.02
Obesity	8.6	11.4	8.4	<0.001
Hypertension, complicated	14.7	3.1	15.4	<0.001
Hypertension, uncomplicated	45.9	26.7	47.1	<0.001
Diabetes with chronic complications	11.2	5.3	11.6	<0.001
Diabetes without chronic complications	11.9	6.9	12.2	<0.001
Peripheral vascular disease	3.2	0.6	3.4	<0.001
Chronic pulmonary disease	21.0	6.0	22.0	<0.001
Drug abuse	20.2	28.9	19.7	<0.001
Median household income by income quartiles (%)				
Q1 (0-25th percentile)	25.5	26.5	25.5	0.28
Q2 (26-50th percentile)	27.1	29.7	27.0	<0.001
Q3 (51-75th percentile)	25.7	26.3	25.6	0.24
Q4 (76-100th percentile)	21.3	17.5	21.5	<0.001
Hospital region (%)				
Northeast	20.7	19.6	20.8	0.28
Midwest	27.4	27.0	27.4	0.93
South	34.1	34.7	34.0	0.13
West	17.8	18.6	17.8	0.41
Primary insurance (%)				
Medicare	54.9	6.8	57.9	<0.001
Medicaid	12.0	35.0	10.6	<0.001
Private insurance	28.1	51.5	26.6	<0.001
Self-pay	2.0	3.9	1.8	<0.001

SD, standard deviation; GERD, gastroesophageal reflux disease; Q, quartile (P≤0.05 indicates significance)

Consistent with findings in upper EAC, smoking and drug use were more prevalent among early-onset patients compared to late-onset middle EAC cases (32.6% vs. 23.7%; P=0.03, and 36.5% vs. 25.5%; P=0.01, respectively). On the other hand, comorbid conditions such as COPD, diabetes mellitus (with and without complications), and hypertension (both complicated and uncomplicated) were more common in late-onset cases compared to early-onset mid-EAC.

No statistically significant differences were observed between early- and late-onset EAC patients in terms of alcohol use, GERD or obesity. Table 3 demonstrates the baseline characteristics of patients with early- vs. late-onset EAC of the mid-third of the esophagus.

Early- vs. late-onset lower EAC

A total of 78,469 hospitalizations for lower EAC were identified, with 6.01% of cases classified as early-onset and 93.98% as late-onset.

The racial distribution showed that most patients were Caucasian, followed by Black and Hispanic individuals. Early-onset EAC cases had a lower proportion of White patients and a higher proportion of Black and Hispanic patients compared to late-onset cases. Similarly to upper and middle EAC, racial distribution significantly differed among early- vs. late-onset lower EAC (P<0.001).

Insurance patterns also differed: early-onset patients were more likely to rely on self-pay, private insurance, or

Table 2 Baseline demographics and comorbidities of patients who were diagnosed with early-onset vs late-onset upper esophageal cancer

Variables	Total upper esophageal cancer	Subdivisions based on age of onset		
		Early-onset	Late-onset	P-value
No. of patients; N (%)	9190 (100%)	585 (6.36%)	8605 (93.63%)	
Age (mean years ±SD)	66.54±0.34	45.05±0.53	68.05±0.30	<0.001
Female sex, (%)	34.32	34.21	34.32	0.97
Race (%)				
Caucasian	63.12	48.65	64.08	0.002
African American	19.70	20.72	19.63	0.58
Hispanic	7.78	13.51	7.4	0.01
Asian or Pacific Islander	4.98	10.81	4.59	0.005
Native American	0	1.01	0.95	0.88
Others	3.47	6.31	3.28	0.04
Comorbidities (%)				
Smoking	22.07	35.09	21.21	0.01
Alcohol use	12.64	19.3	12.2	0.09
GERD with esophagitis	1.85	3.51	1.74	0.33
Obesity	4.25	4.39	4.24	0.95
Hypertension, complicated	13.13	1.75	13.89	<0.001
Hypertension, uncomplicated	44.85	28.95	45.9	0.007
Diabetes with chronic complications	8.07	3.51	8.37	0.13
Diabetes without chronic complications	6.87	7.02	6.86	0.95
Peripheral vascular disease	3.76	1.75	3.89	0.40
Chronic pulmonary disease	24.14	10.53	25.04	0.004
Drug abuse	23.32	36.84	22.43	0.009
Median household income by income quartiles (%)				
Q1 (0-25th percentile)	30.52	30.7	30.5	0.97
Q2 (26-50th percentile)	23.62	21.93	23.74	0.97
Q3 (51-75th percentile)	24.29	23.68	24.33	0.93
Q4 (76-100th percentile)	21.57	23.68	21.42	0.41
Hospital region (%)				
Northeast	22.62	30.7	22.08	0.41
Midwest	24.9	24.56	24.93	0.93
South	34.11	28.95	34.46	0.13
West	18.37	15.79	18.54	0.41
Primary insurance (%)				
Medicare	53.72	1.47	57.49	<0.001
Medicaid	17.84	50	15.52	<0.001
Private insurance	22.89	41.18	21.57	<0.001
Self-pay	2.48	5.88	2.23	0.009

SD, standard deviation; GERD, gastroesophageal reflux disease; Q, quartile (P≤0.05 indicates significance)

Medicaid, while Medicare more frequently covered late-onset patients.

There was no statistically significant difference in the geographic distribution between the 2 groups. However, lifestyle and comorbidity patterns showed distinct trends. Early-onset EAC patients had higher rates of smoking (22.5% vs. 16.2; P<0.001), obesity (13.5% vs. 9.8%; P<0.001), and drug use (26.5% vs. 18.1%; P<0.001). In contrast, late-onset patients had higher prevalence rates of diabetes mellitus (with and without complications), hypertension (complicated and uncomplicated), COPD, and peripheral vascular disease.

No statistically significant differences were observed between early- and late-onset groups in terms of alcohol use or GERD with esophagitis. The baseline characteristics of patients with early- vs. late-onset EAC of the lower third of the esophagus are shown in Table 4.

Discussion

We identified significant disparities in demographics, comorbidities and socioeconomic factors between early- and late-onset EAC. Using a large national inpatient database, we identified trends and disparities that could inform future screening and management strategies.

The racial distribution analysis revealed that early-onset EAC patients had a lower proportion of Caucasian and a higher proportion of Black or Hispanic individuals compared

Table 3 Baseline demographics and comorbidities of patients who were diagnosed with early- vs. late-onset middle esophageal cancer

Variables	Total mid-esophageal cancer	Subdivisions based on age of onset		
		Early-onset	Late-onset	P-value
No. of patients; N (%)	17,569 (100%)	889 (5.06%)	16,680 (94.9%)	
Age (mean years ±SD)	66.39±0.24	43±0.59	67.63±0.21	<0.001
Female sex, (%)	33.66	23.86	34.17	0.002
Race (%)				
Caucasian	64.47	49.12	65.28	<0.001
African American	21.65	35.67	20.90	<0.001
Hispanic	6.65	4.68	6.75	0.14
Asian or Pacific Islander	3.97	8.19	3.75	0.03
Native American	0.53	1.17	0.50	0.22
Others	2.74	1.17	2.82	0.10
Comorbidities (%)				
Smoking	24.13	32.58	23.68	0.03
Alcohol use	13.29	17.42	13.07	0.18
GERD with esophagitis	2.93	2.25	2.97	0.65
Obesity	4.41	5.06	4.38	0.74
Hypertension, complicated	14.88	6.18	15.35	0.006
Hypertension, uncomplicated	44.62	24.16	45.71	<0.001
Diabetes with chronic complications	7.97	3.37	8.21	0.06
Diabetes without chronic complications	8.74	2.25	9.08	0.01
Peripheral vascular disease	3.61	1.12	3.75	0.19
Chronic pulmonary disease	25.21	7.87	26.14	<0.001
Drug abuse	26.07	36.52	25.51	0.01
Median household income by income quartiles (%)				
Q1 (0-25th percentile)	30.90	35.95	30.62	0.31
Q2 (26-50th percentile)	24.72	24.16	24.75	0.97
Q3 (51-75th percentile)	23.59	26.4	23.44	0.93
Q4 (76-100th percentile)	20.79	13.48	21.19	0.13
Hospital region (%)				
Northeast	22.51	15.73	22.87	0.13
Midwest	23.79	33.15	23.29	0.41
South	36.68	33.71	36.84	0.13
West	17.02	17.42	17	0.99
Primary insurance (%)				
Medicare	53.52	12.77	55.62	<0.001
Medicaid	15.81	35.11	14.81	<0.001
Private insurance	25.25	41.49	24.41	<0.001
Self-pay	2.45	7.45	2.19	0.01

SD, standard deviation; GERD, gastroesophageal reflux disease; Q, quartile (P≤0.05 indicates significance)

to late-onset patients. This disparity may reflect differences in healthcare access, socioeconomic status and lifestyle risk factors, such as smoking and alcohol use, which were more prevalent in younger cohorts, as evidenced in our study [8,9]. Okereke *et al* [10] evaluated racial disparities in 127,098 patients with esophageal cancer using the National Cancer Database. As in our study, they found that patients younger than 50 years old had a lower proportion of White individuals and higher proportions of Black and Hispanic individuals compared to older patients.

Early-onset patients had higher rates of smoking, drug use, and obesity than late-onset patients; all these are known to be carcinogenic or proinflammatory factors contributing to esophageal carcinogenesis [11]. This trend underscores the importance of addressing modifiable risk factors in preventive health guidelines targeted toward younger individuals. In contrast, late-onset patients were more likely to present with chronic comorbidities, such as hypertension, COPD and diabetes. These findings are consistent with age-related cumulative exposure to risk factors and comorbidity burden, which may overshadow lifestyle factors in older patients [12]. There is a scarcity of data in the literature describing the baseline characteristics and comorbidities of patients with esophageal cancer, limiting a comparison with our results. A European study [13] evaluated 1243 patients with EAC. Overall, 63% of patients were smokers and 61% had a history of drinking alcohol. In addition, around 23% had hypertension, 10% had diabetes and 18% had pulmonary disease. Another retrospective study involving 682 patients reported that only 1.9% of those under 50 had a Charlson

Table 4 Baseline demographics and comorbidities of patients who were diagnosed with early- vs. late-onset lower esophageal cancer

Variables	Total lower esophageal cancer	Subdivisions based on age of onset		
		Early-onset	Late-onset	P-value
No. of patients; N (%)	78,469 (100%)	4720 (6.01%)	73,749 (93.98%)	
Age (mean years ±SD)	66.57±0.11	43.51±0.25	68.05±10.30	<0.001
Female sex, (%)	17.59	17.18	17.62	0.95
Race, (%)				
Caucasian	84.57	78.56	84.96	<0.001
African American	6.03	8.97	5.85	0.14
Hispanic	4.97	6.67	4.86	0.22
Asian or Pacific Islander	1.71	1.75	1.70	0.77
Native American	0.4	0.77	0.37	0.41
Others	2.32	3.28	2.26	0.41
Comorbidities, (%)				
Smoking	16.59	22.48	16.22	<0.001
Alcohol use	5.42	5.62	5.40	0.81
GERD with esophagitis	2.92	2.23	2.97	0.28
Obesity	10.04	13.47	9.82	<0.001
Hypertension, complicated	14.85	2.76	15.62	<0.001
Hypertension, uncomplicated	46.29	26.94	47.53	<0.001
Diabetes with chronic complications	12.32	5.94	12.73	<0.001
Diabetes without chronic complications	13.18	7.74	13.53	<0.001
Peripheral vascular disease	3.08	0.32	3.25	<0.001
Chronic pulmonary disease	19.72	5.09	20.65	<0.001
Drug abuse	18.56	26.51	18.05	<0.001
Median household income by income quartiles, (%)				
Q1 (0-25th percentile)	24.26	24.25	24.26	0.07
Q2 (26-50th percentile)	28.09	31.68	27.86	0.31
Q3 (51-75th percentile)	26.32	26.62	26.3	0.25
Q4 (76-100th percentile)	21.33	17.46	21.58	0.41
Hospital region, (%)				
Northeast	20.12	18.98	20.19	0.41
Midwest	28.47	26.19	28.62	0.41
South	33.51	35.63	33.38	0.41
West	17.90	19.19	17.82	0.41
Primary insurance, (%)				
Medicare	55.27	6.34	58.4	<0.001
Medicaid	10.53	33.07	9.09	<0.001
Private insurance	29.33	54.65	27.71	<0.001
Self-pay	1.77	2.97	1.7	0.41

SD, standard deviation; GERD, gastroesophageal reflux disease; Q, quartile (P≤0.05 indicates significance)

Comorbidity Index greater than 2, compared to 14% of patients over 50 [7].

The biological explanation of the differences between early- vs. late-onset EAC is still not fully understood. However, it is likely to involve a combination of genetic, molecular and environmental factors that contribute to the disease's distinct pathogenesis and clinical presentation. Genetic polymorphisms in cancer-related genes—particularly those involved in apoptosis, such as *NOS3*, *BCL2*, *TNFRSF10A* and *CASP8*—are significantly associated with early-onset EAC [14]. These genetic factors may contribute to the disease's aggressive nature and earlier development. Molecular characteristics also differ between early-onset and late-onset EAC. Early-onset EAC is more likely to be genomically stable and less likely to exhibit microsatellite instability [15]. This genomic stability may influence tumor behavior and response to treatment.

Many studies in the past have shown early-onset EAC presenting in advanced stages and with poorer outcomes, possibly as a result of delayed diagnosis secondary to a lower index of suspicion for malignancy in younger patients [4,6,7]. Our data are limited to administrative data; therefore, clinical data, such as staging at the time of the diagnosis, could not be collected. However, our study showed that early-onset patients were more likely to rely on Medicaid or self-pay, indicating a lower socioeconomic

status. This aligns with studies highlighting how limited healthcare access and affordability may delay the diagnosis of cancers in younger patients, particularly among marginalized groups [16]. For instance, Black and Hispanic populations often face delays in diagnosis due to the underutilization of screening modalities, resulting in more advanced-stage presentations [10]. Additionally, the greater prevalence of Medicare among late-onset patients underscores the role of established healthcare access in older populations. Similarly, a retrospective study using the Surveillance Epidemiology and End-Results Database, evaluating a total of 12,933 patients with EAC, around 19% of whom were younger than 50 years old, demonstrated poorer survival outcomes with lower household income [17].

Our study has several strengths. Using a national database allowed for robust analyses across multiple demographic and clinical variables. We compared early- and late-onset cases across different EAC anatomical subtypes; hence, the study provides nuanced insights into age-related differences in disease characteristics stratified by anatomic subtype. Using a nationwide database enhances the generalizability of findings to hospitalized patients across the United States.

However, this study has several limitations. First, NIS provides data from hospital admissions and does not capture outpatient treatments, which are increasingly common for EAC patients. Therefore, our results may not be generalizable to those treated exclusively in outpatient or ambulatory care settings. Second, the data are limited to administrative codes, such as ICD-10-CM, which may lead to the misclassification or under-coding of certain conditions. For the same reason, data pertinent to staging are missing. Third, The NIS does not include detailed clinical information, such as laboratory values, imaging findings or specific treatment regimens, which could provide insights into the relationship between predictors and EAC. Despite these limitations, our study provides valuable insights into the variability of characteristics among hospitalized early- vs. late-onset EAC patients, emphasizing the need for improved vigilance.

In conclusion, our study identified significant differences in demographics and risk factors between early- and late-onset EAC. These findings emphasize the need for tailored preventive strategies and more inclusive screening practices. Further research is crucial to understand the disparities better and improve outcomes in younger populations.

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Summary Box

What is already known:

- Esophageal adenocarcinoma (EAC) is uncommon in individuals under 50, but has shown a rising incidence in this age group
- Younger patients with EAC are more likely to present at advanced stages, and have poorer prognoses compared to older individuals

What the new findings are:

- Early-onset EAC represents approximately 6% of all hospitalized EAC cases, and shows significant differences in racial, clinical and socioeconomic characteristics compared to late-onset EAC
- Younger patients had higher rates of smoking, obesity and drug use, but fewer chronic comorbidities such as hypertension, diabetes and chronic obstructive pulmonary disease
- Early-onset patients were more often covered by Medicaid, or were uninsured, and were less likely to be on Medicare, suggesting disparities in healthcare access
- These findings highlight the need for revised screening strategies and targeted prevention efforts in younger, at-risk populations

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