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Original Article

Inpatient burden of esophageal cancer and analysis of factors affecting in-hospital mortality and length of stay

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SUMMARY. **Esophageal cancer (EC) continues to be a major source of morbidity and mortality in the United States. However, there has been a relative dearth of research into hospital utilization in patients with EC. This study examines temporal trends in hospital admissions, length of stay (LOS), mortality, and costs associated with EC. In addition, we also analyzed factors associated with inpatient mortality and LOS. We interrogated National Inpatient Sample (NIS), a large registry of inpatient data, to retrieve information about various demographic and factors associated with hospital stay in patients who were admitted for EC between the years 1998 and 2013 in the United States. After examining trends over time, multivariate analysis was performed to identify factors associated with LOS and mortality. During 1998–2013, 538,776 hospital stays with principal diagnosis of EC were reviewed. Number of hospital stays and inpatient charges increased by 397 per year (±67.8; $P < 0.0001$) and $3,033 per patient per year (±135; <0.0001) respectively. Mortality and LOS decreased by 0.23% per year (±0.03; $P < 0.0001$) and 0.07 days per year (±0.006; $P < 0.0001$) respectively. Multiple factors associated with LOS and mortality were outlined. Despite overall increase in hospital utilization with respect to number of admissions and inpatient charges, inpatient mortality and LOS associated with EC declined. Factors associated with inpatient mortality and LOS may help drive clinical decision-making and influence healthcare or hospital policy.**

KEY WORDS: **cancer epidemiology, esophageal adenocarcinoma, esophageal cancer, length of stay, inpatient costs, inpatient mortality.**

INTRODUCTION

Esophageal cancers (ECs) represent a small portion of gastrointestinal malignancies but portends a poor prognosis.[1] In the United States, 16,910 new cases of EC were diagnosed in 2016, accounting for approximately 5.5% of all new cases of gastrointestinal cancers. Historically, esophageal squamous cell carcinoma accounted for majority of EC in United States, but since 1960s there has been a shift in the histological type. Owing to rising rates of obesity, proportion of EC related to esophageal adenocarcinoma has doubled from 35% to 61% in the last 30 years.[2]

Despite emergence of surgical and endoscopic techniques,[3,4] and advances in targeted therapeutics,[5] mortality associated with EC continues to rise.[6] This may be related to advanced stage of EC at the time of EC diagnosis.[6] A total of 15,690 deaths (12,720 in men) were related to EC in 2016, which is roughly equivalent to 10% of all deaths from gastrointestinal cancers.[1] EC is the seventh leading cause of cancer death among men in the United States.[7]

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In 2015, approximately 1.5 billion dollars were spent taking care of patients with EC.[8] Almost half of this cost—around 700 million dollars—was spent during the last year of life of the patients.[8] Although previous studies have demonstrated that majority of expense in end-of-life setting for most cancers is related to inpatient costs, relatively little is known about the inpatient costs in EC.[9] In fact, there has been a relative dearth of research into inpatient burden of EC. In this study, we used the NIS database—the largest all-payer inpatient database in the United States containing data from approximately 8 million hospital stays each year— to evaluate characteristics and trends in hospital utilization in patients with EC. In addition, we evaluated the risk factors associated with inpatient mortality, length of stay (LOS), and inpatient charges.

METHODS

National Inpatient Sample and inclusion criteria

Nationwide Inpatient Sample (NIS) is the largest available all-payer inpatient database that approximates data from 20% of the hospitalizations in the United States. NIS was developed by Agency for Healthcare Research and Quality as part of the Health Care and Utilization Project (HCUP). We studied NIS data between 1998 and 2013 to obtain frequency of hospital stays where the primary diagnosis was EC in patients with age of 18 or higher using ICD-9 codes (150.0150.1150.2150.3, 150.4, 150.5, 150.8, 150.9, 230.1, V1003). Patients in the NIS database not meeting the aforementioned ICD-9-CM criteria and patients in the NIS database who were not hospitalized between the years 1998 and 2013 were excluded from further analysis.

Trends in hospital-associated characteristics

Incidence of hospital stays per 100,000 US population per year was obtained by dividing the number of hospital stays for each year by the US population corresponding to that year.[10] Further, data regarding LOS, cost per admission, and inpatient mortality rate were also obtained. Linear regression analysis yielded changes in variables per year along with 95% confidence intervals (CIs). LOS was defined as the number of nights the patient remained in the hospital for this stay. Cost per admission was defined as hospital charges for the entire hospital stay. Inpatient mortality rate was defined as number of inpatient deaths divided by number of hospital stays for each year.

Analysis of factors associated with mortality, length of stay, and costs

To examine the risk factors associated with LOS and inpatient mortality rate, multivariate analysis was performed. Variables examined as part of the multivariate analysis included multiple patient demographic characteristics and characteristics related to hospitalization. The following patient characteristics were examined: sex (male or female), age (grouped as 18–45, >45–65, >65–85, and >85 years), smoking, personal history of alcohol use, payer type (Medicare, Medicaid, private insurance, or self-pay), Charlson morbidity score, and patient's residence in specific zip-code (grouped by median income of that zip-code: 0–25th percentile, >25th–50th percentile, >50th–75th percentile, >75th–100th percentile).

Hospitalization related characteristics including, and hospital size (characterized as small, medium, and large), teaching versus nonteaching status, and hospital location (Metropolitan versus non-Metropolitan) were examined. As the definition of hospital size varied according to the hospital location and teaching status, the following ranges were identified for small (1–299 bed), medium (50–499 beds), and large (100 to >500 beds) hospitals. Metropolitan areas were defined as hospitals located in areas with at least 50 000 people. Hospital stay characteristics such as admission during weekend (defined as admission during Saturday–Sunday), elective nature of the admission, complications during hospital stay (development of acute kidney injury or acute respiratory failure), and hospital stays involving transfer to intensive care unit were also examined using multivariate analysis to understand their effect on LOS and inpatient mortality.

RESULTS

Trends in hospital-associated characteristics

From 1998 to 2013, there were 538,776 hospital discharges with a principal diagnosis of EC. Number of hospital stays per year, in-hospital mortality rate, LOS, and aggregate inpatient charges for EC over this period were tabulated in Table 1 and displayed graphically in Figures 1–5. Linear regression of number of hospital discharges demonstrated an overall increase in number of discharges by 397 per year (±67.8; $P < 0.0001$). Number of discharges for EC ranged from a minimum of 30,709 in 2000 to a maximum of 37,402 in 2009. Stratified-analysis using linear regression revealed an increase in discharge rate of 481 per year (±97; $P = 0.0006$) between the years 1998 and 2009. However, from the years 2009 to 2013, there was a significant decrease in discharge rate by 834 per year (±171; $P = 0.04$). However, the data on incidence of hospitalization per 100,000 between 1998 and 2013 have not shown a statistically significant increase (0.03 per 100,000 US population per year ±0.02; $P = 0.248$). The maximum incidence of 12.2 per 100,000 US population occurred in year 2009

Table 1. Trends in various characteristics related to inpatient related to esophageal cancer

Year	Hospital stays per year	Hospitalization rate†	Mortality†	Length of stay†	Cost per stay†
1998	32,263 ± 2036	11.7 ± 0.7	13% ± 0.5	8.1 ± 0.2	$21,124 ± 767
1999	31,599 ± 1932	11.3 ± 0.7	12.3% ± 0.7	7.9 ± 0.2	$22,990 ± 1359
2000	30,709 ± 1756	10.9 ± 0.6	11.5% ± 0.7	7.9 ± 0.2	$24,501 ± 916
2001	30,802 ± 1764	10.8 ± 0.6	11.7% ± 0.5	8.1 ± 0.2	$28,458 ± 1139
2002	31,408 ± 1911	10.9 ± 0.7	11.1% ± 0.4	7.8 ± 0.2	$30,600 ± 1288
2003	31,585 ± 1978	10.9 ± 0.7	10.2% ± 0.5	7.8 ± 0.2	$36,947 ± 2346
2004	32,720 ± 2049	11.2 ± 0.7	11.1% ± 0.4	7.6 ± 0.2	$34,007 ± 1323
2005	33,277 ± 1868	11.3 ± 0.6	10.1% ± 0.4	7.6 ± 0.1	$38,314 ± 2176
2006	33,192 ± 1852	11.1 ± 0.6	11.1% ± 0.4	7.5 ± 0.2	$40,171 ± 1522
2007	35,665 ± 2139	11.8 ± 0.7	9.4% ± 0.4	7.4 ± 0.2	$44,708 ± 2367
2008	34,658 ± 2102	11.4 ± 0.7	10.2% ± 0.4	7.6 ± 0.1	$51,209 ± 2841
2009	37,402 ± 2242	12.2 ± 0.7	9.6% ± 0.4	7.3 ± 0.1	$50,711 ± 2201
2010	37,280 ± 2419	12 ± 0.8	9% ± 0.4	7.3 ± 0.2	$55,919 ± 2463
2011	36,271 ± 2349	11.6 ± 0.8	9.2% ± 0.4	7.2 ± 0.2	$64,555 ± 5557
2012	35,030 ± 933	11.1 ± 0.3	9.5% ± 0.4	7.2 ± 0.1	$61,711 ± 1729
2013	34,915 ± 979	11 ± 0.3	9.2% ± 0.4	6.8 ± 0.1	$62,814 ± 1847

†Hospitalization rate expressed as patients per 100,000 US population for that year, mortality expressed as percent died during hospital stay, length of stay in days, and inpatient charges in dollars. Each variable expressed with ± standard error.

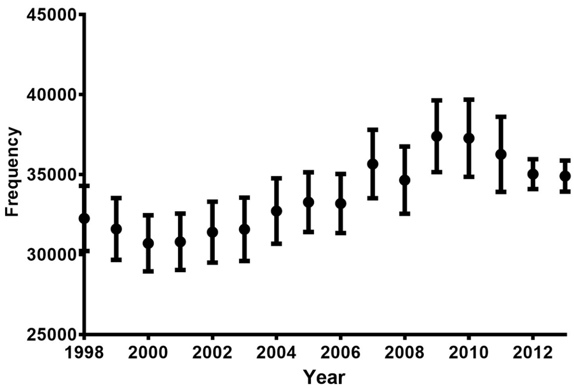

Fig. 1 Frequency of hospital stays per year (represented by dots) along with the corresponding 95% confidence intervals are shown from 1998 to 2013.

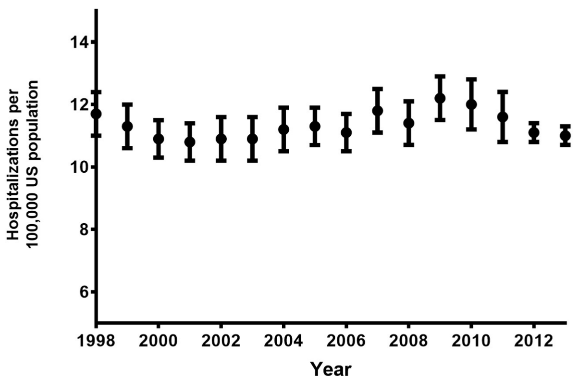

Fig. 2 Hospitalizations per 100,000 US population per year (represented by dots) along with the corresponding 95% confidence intervals are shown from 1998 to 2013.

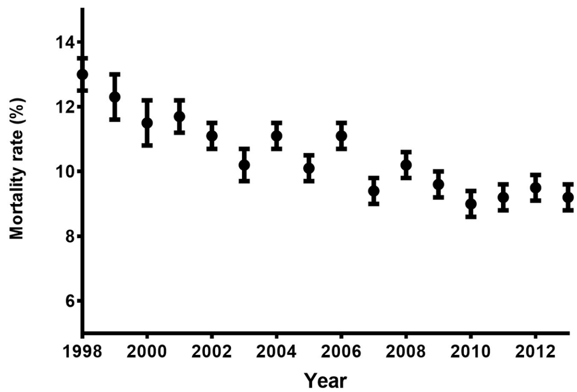

Fig. 3 In-hospital mortality rate per year (represented by dots) along with the corresponding 95% confidence intervals are shown from 1998 to 2013.

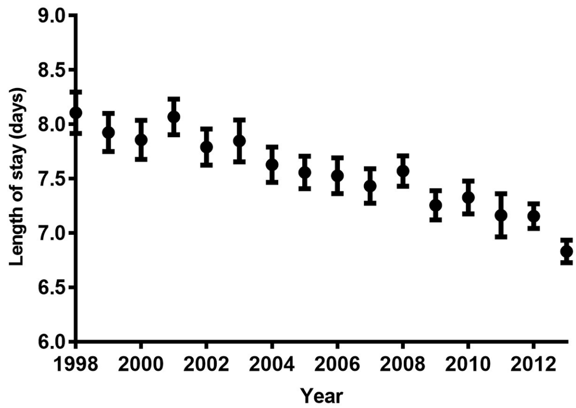

Fig. 4 Average length of stay per year (represented by dots) along with the corresponding 95% confidence intervals are shown from 1998 to 2013.

and corresponded to maximum number of discharges noted above. The minimum incidence was 10.8 per 100,000 US population and occurred in the year 2001. Stratified analysis of incidence also did not show a statistically significant increase in incidence between 1998 and 2009 (0.05 per 100,000 US population per year ±0.03; $P = 0.13$). However, stratified analysis of incidence noted a significant decrease in incidence from 2009 to 2013 by 0.33 per 100,000 US population per year (±0.04; $P = 0.0028$).

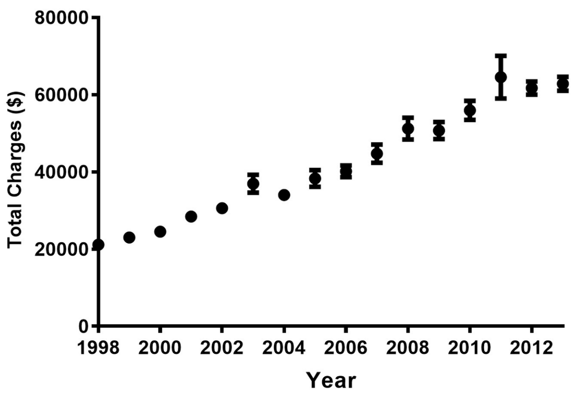

Fig. 5 Average inpatient charges per patient per year (represented by dots) along with the corresponding 95% confidence intervals are shown from 1998 to 2013.

With regards to mortality, there was an overall decrease of 0.23% per year (±0.03; $P < 0.0001$) between 1998 and 2013. The highest mortality was noted in the year 1998 (13% ± 0.5), and the lowest mortality was noted in the year 2010 (9% ± 0.4). Stratified linear regression analysis between the years 1998 and 2010 revealed a decrease in mortality of 0.27% per year (±0.04%, $P < 0.0001$). However, similar analysis between the years 2010 and 2013 demonstrated a nonsignificant increase of 0.03% per year (±0.16; $P = 0.888$).

Inpatient charges for EC between 1998 and 2013 increased by $3033 per year (±135; <0.0001). Adjusting for inflation by converting costs to 2013 dollars demonstrates an increase of $2411 (±140; $P < 0.0001$). The maximum unadjusted cost per hospitalization occurred in the year 2010 ($64,555), and the minimum cost occurred in the year 1998 ($21,124). Adjusting to 2013 dollars, the minimum cost per hospitalization occurred in 1998 ($30,101), and the maximum cost per hospitalization occurred in 2010 ($67,503). LOS showed a steady decline of 0.07 days per year (±0.006; $P < 0.0001$) from 1998 (8.1 days) to 2013 (6.8 days).

Factors associated with inpatient mortality

Multivariate analysis of factors associated with inpatient mortality is displayed in Table 2. Patients in age group 65–84 ((OR 1.4 (95%CI 1.1–1.8) $P = 0.0035$) and over 85 (OR 1.8 (95%CI 1.4–2.4) $P < .0001$) had greater rate of mortality compared to those admitted between ages 18 and 44. Compared to Medicare beneficiaries, patients who had Medicaid (OR 1.4 (95%CI 1.2–1.7) $P < .0001$), private insurance (OR 1.6 (95%CI 1.5–1.9) $P < .0001$), and self-pay (OR 2.6 (95%CI 2.1–3.1) $P < .0001$) had higher rates of inpatient mortality. Other factors associated with increased inpatient mortality rate include admission during a weekend (OR 1.1 (95%CI 1.0–1.2) $P = 0.0298$), hospitalization involving critical care unit stay (OR 2.934 (95%CI 2.509–3.429) $P < .0001$), acute kidney injury (OR 2.209 (95%CI 2.002–2.436) $P < .0001$), acute respiratory failure (OR 5.544 (95%CI 5.01–6.136) $P < .0001$), and Charlson comorbidity score of >1 (OR 1.137 (95%CI 1.119–1.156) $P < .0001$). Factors that associated with decreased in hospital mortality include history of smoking (OR 0.7 (95%CI 0.6–0.8) $P < .0001$), history of alcohol abuse (OR 0.8 (95% CI 0.7–0.9) $P < .0001$), and discharge from teaching hospital (OR 0.8 (95%CI 0.7–0.9) $P < .0001$).

Factors associated with length of stay

Multiple factors were associated with LOS as shown in Table 2. GC patients who are males stayed 0.58 days (±0.08; $P = <.0001$) longer than females. Patients living in zip-codes where median income was between >75th–100th percentile stayed 0.29 days (±0.13; p 0.0232) longer than those living in zip-code where the median income was between 0 and 25th percentile. Patients with personal history of alcohol abuse stayed 0.98 days (±0.14; $P < .0001$) longer. Patients admitted to metropolitan hospitals, large hospitals, or teaching hospitals stayed 1.04 days (±0.12; $P < .0001$), 1.03 days (±0.14; $P < .0001$), and 0.94 days (±0.1; $P < .0001$) longer than those admitted to non-metropolitan hospitals, small hospitals or non-teaching hospitals, respectively. Having an elective admission resulted in increased LOS by 2 days (±0.13; $P < .0001$). Hospital stay being complicated by an ICU stay, acute kidney injury, or acute respiratory failure resulted in increased hospital stay by 13.03 days (±0.45; $P < .0001$), 2.24 days (±0.15; $P < .0001$), and 3.44 days (±0.17; $P < .0001$) respectively.

On the other hand, having private insurance, being black, being admitted during a weekend or having personal history of smoking reduced LOS by 0.53 days (±0.1; $P < .0001$), 0.8 days (±0.22; p 0.0002), 0.29 days (±0.07; $P < .0001$), and 0.95 days (±0.07; $P < .0001$) compared to those having Medicare insurance, being Caucasians, being admitted during weekdays or not having personal history of smoking.

DISCUSSION

The purpose of this study is to understand the data associated with inpatient stays associated with EC. This study specifically looked at variables such as incidence of hospitalizations, LOS, mortality, costs related to hospitalizations, and basic demographic information among hospitalized EC patients over a period of 16 years (1998–2013). Per absolute numbers in the NIS database, there was a statistically significant increase in number of hospital stays per year from 1998 to 2009, with a subsequent decrease in absolute number of hospital stays per year between 2009 and 2013. However, controlling for population growth by

Table 2. Multivariate analysis of patient demographic characteristics as they relate to hospital mortality and length of stay

Variable	Reference	Variable	Mortality (1)†	LOS (2)†	*P* value
Sex	Male	Female	1 (0.9–1.1)	0.58 ± 0.08	1-<.0001 2-<.0001
Age	18–44	45–65	1 (0.8–1.3)	0.02 ± 0.21	1-0.4848 2-0.9358
		65–84	1.4 (1.1–1.8)	−0.14 ± 0.24	1-0.9056 2-0.5595
		>84	1.8 (1.4–2.4)	−0.41 ± 0.27	1-0.0035 2-0.1214
Payer	Medicare	Medicaid	1.4 (1.2–1.7)	0.23 ± 0.16	1-<.0001 2-0.1438
		Private insurance	1.6 (1.5–1.9)	−0.53 ± 0.1	1-<.0001 2-<.0001
		Self-pay	2.6 (2.1–3.1)	−0.26 ± 0.15	1-<.0001 2-0.0756
Race	Caucasian	Black	1.1 (1–1.3)	−0.8 ± 0.22	1-<.0001 2-0.0002
		Hispanics	1 (0.9–1.2)	0.34 ± 0.24	1-0.0965 2-0.1554
		Other	1 (0.9–1.2)	−0.37 ± 0.27	1-0.9215 2-0.1749
Zip code based on income	0–25th percentile	26th to 50th percentile	1 (0.9–1.1)	0.15 ± 0.1	1-<.0001 2-0.1134
		51st to 75th percentile	1 (0.9–1.1)	0.16 ± 0.1	1-0.3818 2-0.1317
		76th to 100th percentile	1 (0.9–1.2)	0.29 ± 0.13	1-0.9282 2-0.0232
Hospital-associated characteristics					
Urban Location	No	Yes	0.7 (0.6–0.8)	1.04 ± 0.12	1-0.6337 2-<.0001
Teaching Hospital	No	Yes	0.8 (0.7–0.9)	0.94 ± 0.1	1-<.0001 2-<.0001
Admission during weekend	No	Yes	1.1 (1–1.2)	−0.29 ± 0.07	1-<.0001 2-<.0001
Elective admission	No	Yes	0.6 (0.5–0.7)	2 ± 0.13	1-0.0298 2-<.0001
Hospital bed size	Small	Medium	0.9 (0.8–1)	0.41 ± 0.16	1-<.0001 2-0.008
		Large	0.8 (0.7–0.9)	1.03 ± 0.14	1-0.1789 2-<.0001
Comorbidities					
Smoking	No	Yes	0.7 (0.6–0.8)	−0.95 ± 0.07	1-<.0001 2-<.0001
Alcohol abuse	No	Yes	0.8 (0.7–0.9)	0.98 ± 0.14	1-<.0001 2-<.0001
Required ICU stay	No	Yes	2.9 (2.5–3.4)	13.03 ± 0.45	1-0.0058 2-<.0001
Acute kidney injury	No	Yes	2.2 (2–2.4)	2.24 ± 0.15	1-<.0001 2-<.0001
Acute respiratory failure	No	Yes	5.5 (5–6.1)	3.44 ± 0.17	1-<.0001 2-<.0001
Morbid obesity	No	Yes	0.6 (0.5–0.7)	0.23 ± 0.15	1-<.0001 2-0.1274
Charlson comorbidity score	≤2	>2	1.1 (1.1–1.2)	0.03 ± 0.02	1-0.731 2-0.0669

†Inpatient mortality for each category is expressed as odds ratio with 95% confidence intervals in parentheses. For length of stay (LOS), correlation coefficient for each category was listed with standard error.

reorganizing the frequency of hospital stays as incidence of hospitalizations per 100,000 US population for the corresponding years, there was no substantial change in incidence of hospitalizations between 1998 and 2009. However, corresponding with the drop in absolute number of hospital stays between 2009 and 2013, there was also a significant drop in the incidence of hospital stays per 100,000 US population of during this period.

This analysis of hospitalization trends roughly corresponds to a recent NIS analysis, demonstrating a 4% decrease in adult hospital stays principally for cancer of any cause between the years 2000 and 2009.[11] In contrast to the trends in hospital stays noted in our study, the overall incidence of EC in United States as well as other Western populations is on the rise.[12] The overall increase in EC incidence may be attributable to an increase in rates of obesity, gastroesophageal reflux, and tobacco smoke, all major risk factors in development of EC—especially when they occur together.[13] The discrepancy between the overall stabilization or decrease in hospital stays but increase in EC incidence may be explained by growing outpatient cancer treatment options[11] and increasing use of palliative medicine services for end of life care which in many studies have shown reduction in hospitalization usage.[14]

Mean LOS for all-cause hospitalizations during this period decreased by 4.8%, and mean LOS for EC decreased by 19.1%. Increased awareness and utilization of home care services over the last decade has likely contributed to this improvement in LOS.[15] For example, a patient who needed to stay in the hospital for management of total parenteral nutrition in the setting of failure to thrive, or a patient who is in the hospital due to difficulty with activities of daily living, can now be managed by home health agencies. Further, increased usage of palliative medicine services might also be associated with a lower LOS.[14]

As noted in Table 2 many factors were associated with minute but statistically significant LOS. When hospital course was complicated by an ICU stay, acute respiratory failure, acute kidney injury, a greater LOS was noted. This trend is not limited to EC admissions.[16] In terms of hospital characteristics, Medicare patients experienced greater LOS compared to those with private insurance. Medicare's 3-day rule, which requires 3 days of hospital stay before Medicare will pay for transfer to postacute rehabilitation facility is likely responsible for this discrepancy. This phenomenon has been described with other causes of hospitalizations,[17] suggesting need for revision of this rule. While higher LOS was associated with male gender, consistent with previous data, higher LOS associated with high income communities is not consistent with previous data.[18]

The average cost of hospitalization for EC increased by a staggering 100.8%. Multiple factors may have contributed to this substantial increase in costs associated with EC hospitalization. Examination of Medicare beneficiaries with cancer from 1999 to 2006 has revealed significant increase in use of imaging modalities like positron emission tomography, bone density studies, echocardiograms, magnetic resonance imaging, and ultrasounds among all cancer types.[19] In late 1990s, surgery (en-bloc resection, extended field lymphadenectomy, trans-hiatal esophagectomy), radiotherapy, chemotherapy (5-FU and cisplatin), and combination of these therapies were the primary modalities of treatment for EC.[20] A number of newer and more expensive treatment and palliation options have spawned since 1990s, including intensity-modulated radiation therapy, 3D-conformational radiation therapy, and esophageal stents.[21] Further, while incidence of localized EC has remained stable over this time, incidence of advanced stage EC has risen significantly.[6] Although these data are not available for EC, in other cancer types, it was noted that the costs of treating advanced stage cancers are significantly higher than treating patients with localized cancers.[22] Together, changes in cancer diagnostics and therapeutics, along with increased incidence of advanced stage cancers over this time may explain the steep increase in inpatient hospital costs noted in this study.

While these advances have added to costs, advancements in our understanding of cancer biology, in various new treatment modalities, and improved access to up-to-date medical care, have led to an increasing trend of five year survival rate in EC.[23] Inpatient mortality rate in this study has decreased 2.9% consistent with overall improvement in morality in EC.[24]

As noted in previous studies, older age groups, patients whose hospital course was complicated by ICU stay, acute kidney injury, acute renal failure, and those with high Charlson index had higher rate of mortality.[25-27] Interestingly, compared to Medicare patients, Medicaid, private, and self-pay patients had higher mortality rate. Reasons for this trend are not clear, but one explanation could be that Medicare patients better access and more continuous insurance coverage compared to those with other types of insurance.[28,29]

Although use of the NIS database has allowed examination of larger trends in EC, it is important to understand some of the limitations of using these data. NIS database was interrogated using specific ICD-9 code for EC. Erroneous data entry or omissions in coded data could have resulted in unintended exclusion of patients with EC. Additionally, this could have led to errors in various variables that were examined in this study such as costs, hospital mortality, costs, or other demographic information. Research on accuracy of coding practices is needed to help verify the accuracy of data presented in this study. NIS also limits the type of data that can be examined. For example, procedures and treatments the patient underwent, especially if in different healthcare facilities, would be hard to examine using NIS.

CONCLUSION

Esophageal cancer is associated with significant morbidity and mortality. This study examined the inpatient burden of EC and characteristics of hospital utilization in patients with EC using NIS, a large all-payer inpatient database. Although there was an overall increase in hospital stays and mortality during the study period, stratified analysis noted a significant decrease in hospital stays and a nonsignificant decrease in inpatient mortality from 2009 and 2010 onwards, respectively. LOS continued to decline, and inpatient charges continued to rise throughout the study period. Multiple characteristics such as age, gender, patients' zip-code (as it relates to median income of the zip-code), alcohol abuse, smoking status, type of hospital, size of hospital, hospital course being complicated by either an ICU stay, acute kidney injury, or acute respiratory failure, being admitted during a weekend, type of insurance, race, and number of comorbidities seem to affect LOS and inpatient mortality.

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