Research Article

Cancer Epidemiology, Biomarkers & Prevention

Individual- and Area-Level Socioeconomic Inequalities in Esophageal Cancer Survival in Shandong Province, China: A Multilevel Analysis

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Abstract

Background: China contributes to almost half of the esophageal cancer cases diagnosed globally each year. However, the prognosis information of this disease in this large population is scarce.

Methods: Data on a population-based cohort consisting of residents of Shandong Province, China who were diagnosed with esophageal cancer during the period from 2005 to 2014 were analyzed. The cancer-specific survival rates were estimated using Kaplan–Meier analysis. Discrete-time multilevel mixed-effects survival models were used to investigate socioeconomic status (SES) disparities on esophageal cancer survival.

Results: The unadjusted 1-, 3-, and 5-year cause-specific survival rates were 59.6% [95% confidence interval (CI), 59.2%–59.9%], 31.9% (95% CI, 31.5%–32.3%), and 23.6% (95% CI, 23.1%–24.0%), respectively. Patients of blue-collar occupations had higher risk of esophageal cancer–related death than those of white-collar occupations in the first 2 years after diagnosis. Rural patients had higher risk of death than urban patients in the first 3 years after diagnosis. The risks of esophageal cancer–related death among patients living in low/middle/high SES index counties were not different in the first 2 years after diagnosis. However, patients living in high SES index counties had better long-term survival (3–5 years post-diagnosis) than those living in middle or low SES index counties.

Conclusions: Socioeconomic inequalities in esophageal cancer survival exist in this Chinese population. Higher individual- or area-level SES is associated with better short-term or long-term cancer survival.

Impact: Elucidation of the relative roles of the SES factors on survival could guide interventions to reduce disparities in the prognosis of esophageal cancer.

Introduction

China has the highest incidence rate of esophageal cancer in the world, contributing almost half of the esophageal cancer cases diagnosed globally in 2012 (1). However, prognosis information for this large group of patients with esophageal cancer is scarce. A national-level study reported the 5-year relative survival rate of esophageal cancer is 20.9%–30.3% during 2003–2015 (2). These estimates were based on data from only 17 cancer registries covering less than 2% of the Chinese population (3).

International studies about the influence of socioeconomic status (SES) on esophageal cancer survival have reported conflicting results. The majority of the literature has pointed to a consistent relationship between SES and esophageal cancer survival, with patients in lower social classes or living in deprived areas having consistently poorer survival than those in higher social classes or living in affluent areas (4–9). However, others have reported that esophageal cancer survival was not associated with SES or urban/rural residential type after adjustment for individual's characteristics and cancer treatment (10–12). The role of individual-level and area-level SES factors on esophageal cancer survival in the Chinese population has not yet been well elucidated. The national-level study suggested that the survival of esophageal cancer was better for rural patients than urban patients, in contrast to the better survival outcomes for urban patients diagnosed with other cancers (2). In addition, the few studies which have evaluated the role of SES factors in cancer survival have considered individual and area effects simultaneously using a model that allows for SES variables over multiple levels.

Shandong Province lies in the "Asian esophageal cancer belt," which has the highest incidence of this disease (13). It is the second most populous province in China, with 98.5 million people accounting for 7.2% of the Chinese population (3). Before 2005, cancer registration was performed by only two counties in Shandong, meaning that estimates of cancer survival were severely limited. To date, the survival rate of esophageal cancer and associated factors have never been reported at the provincial level in Shandong.

We have previously identified a high-mortality cluster in Shandong, with residents living in the cluster area being 3.7 times more likely to die from esophageal cancer than residents in the rest of Shandong (14). Whether the high mortality in this cluster area is

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due to poorer survival for the patients with esophageal cancer living in the area remains unknown. This study aims to quantify the survival characteristics for people diagnosed with esophageal cancer in Shandong Province and explore the potential association between SES factors and esophageal cancer survival, particularly in the high-mortality cluster area. It is hoped that the results of this study will inform efforts to improve early detection and more effective treatment of this disease.

Materials and Methods

Study site and unit of analysis

There are 142 county-level units (small cities/counties/districts) covering Shandong Province without gaps or overlap (15). The Shandong population is highly homogeneous in terms of ethnicity, with 99.3% of the population belonging to the Han ethnic group (16). Variation in esophageal cancer survival was analyzed according to the hierarchical structure where individuals (level 1) were nested within subcounty units (level 2, $n = 262$) within county-level units (level 3, $n = 142$).

Survival data and data quality

Cancer registration data were extracted from Shandong Cancer Registration System (SCRS). SCRS was established in 2005, initially collecting incident cancer cases and follow-up information from 49 counties in Shandong. The population coverage of SCRS continued to increase so 130 counties were included in 2014 (Supplementary Fig. S1).

The methods for case ascertainment and data collection in the SCRS have been reported previously (17). In brief, new diagnoses were reported by local hospitals, community health service centers, the Urban Residents Basic Medical Insurance program, and the New-Rural Cooperative Medical System. These cases were then followed for vital status until death or loss of follow-up (17).

Both active and passive methods were used for patient follow-up. On a yearly basis, usually in the first few months, the county-level Centers for Disease Control and Prevention (CDC) organized active investigations for all the registered patients with cancer from their catchment area whose current vital status is "alive." Public health workers and doctors in the communities were involved in the investigations, as they often have detailed information on the vital status of the patients. When the vital status was unknown by the public health workers and doctors, face-to-face or telephone interviews were conducted with the patients or family members. The follow-up results including vital status ("alive," "dead," or "loss of follow-up"), date of follow-up, and when applicable, date of death were then entered into the registration system.

In addition, vital status including date of death and cause of death from Shandong Death Registration System (SDRS) are routinely used to update the follow-up status in SCRS (passive follow-up). Cause-of-death information from SDRS was collected on the basis of a national standard protocol and was double checked by physicians and their direct managers within 7 days after death registration (18). Vital status of migrant workers from rural areas was collected mainly by enquiring their local family members or neighbors, and by linkage with the SCRS data. By law, all deaths should be registered in their original residence.

The Shandong CDC checked and evaluated the quality and comparability of the submitted cancer registration data based on "Guideline for Chinese Cancer Registration" and referring to relevant data quality criterion of "Cancer Incidence in Five Continents Volume IX" by International Agency for Research on Cancer/International Association of Cancer Registries (IARC/IACR; refs. 17, 19). The IARC/IACR Check Program was used for internal consistency checks to detect unlikely or implausible combination of codes (17). For patients with esophageal cancer in this study, the percentage of death certificate–only cases for the SCRS data was 1.8%.

Incident cases of malignant neoplasm of the esophagus (ICD-10 code: C15) diagnosed between January 1, 2005 and December 31, 2014 were extracted from the SCRS ($n = 79{,}873$). The study cohort was followed up to December 31, 2016. Cases who were aged <20 years at diagnosis ($n = 158$), who had an invalid address code ($n = 1{,}091$), missing follow-up information ($n = 10{,}482$), survived less than 1 day ($n = 1{,}812$), or who had incomplete cause-of-death information ($n = 905$) were excluded, given the final study cohort of 65,425 cases. The survival time was truncated at 5 years postdiagnosis for all cohort members.

Because the cancer registration system is new to many counties and there are delays in organizing the yearly active follow-up, the cohort diagnosed in most recent years has a higher chance of missing follow-up information. Multivariable logistic regression comparing the characteristics of the excluded patients with missing follow-up data to those of the final study cohort showed that patients diagnosed between 2013 and 2014 were 7.4 [95% confidence interval (CI), 6.1–9.0] times more likely to be excluded from final analysis, with 74% of the missing follow-up cases being diagnosed between 2013 and 2014 (Supplementary Table S1). Therefore, a sensitivity analysis which excluded all patients diagnosed between 2013 and 2014 was conducted to see whether the main findings were robust for the 2005–2012 cohort.

Measurement of occupation (individual-level SES)

Occupation data are based on the patient's job at the time of diagnosis. Occupation information was coded by the second edition of the Chinese Standard Classification and Codes of Occupations (20). The Chinese Standard Classification and Codes of Occupations is a skill-based measure that groups occupations requiring similar levels of education, knowledge, responsibility, on-the-job training, and experience. It comprises eight occupation categories: (i) managers, (ii) professionals, (iii) government officers, (iv) service and sales workers, (v) skilled agricultural, forestry, and fishery workers, (vi) laborers and craft workers, (vii) armed forces occupations, and (viii) others. We recoded the occupation information into four categories for analyses as follows: white-collar employees (1–4, and 7), blue-collar workers (5 and 6), others (8), and unknown (patients without occupation code). The percentage of the blue-collar residents for the final study cohort (76%) was higher than the percentage in the general Shandong population (58%) in 2009 (ref. 21; Supplementary Table S2), consistent with previous studies showing that lower socioeconomic class was related to higher esophageal cancer incidence (22, 23).

Measurement of residential type (subcounty-level SES)

Residential type (urban/rural) has been chosen as the subcounty-level SES variable in this study. We classified residential type according to the national standards of urban and rural deviation (24). Briefly, in county-level units, subdistricts, consisting of urban communities or neighborhoods clustered around the center of the county-level units were classified as urban areas;

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and townships, consisting of a town center and the surrounding villages were classified as rural areas. More information about the residential type classification in Shandong has been published previously (15). Studies have reported that in China, rural residents on average have lower SES than urban residents (25).

The urban/rural classification approach applied in this study is different from the approach applied in the national survival study (2), which classified residential type at county level, where only the districts of major cities were considered to be urban, while small cities or counties were considered to be rural. In fact, about one-third of the residents in small cities or counties actually reside in urban communities (24). For purposes of comparison, we also did data analysis using the county-level classification approach.

Measurement of SES index (county-level SES)

The county-level SES variables considered in this study were average gross domestic product (GDP) per capita, average years of school education for adults, and hospital beds to population ratio. The 2011–2013 data for these measurements were extracted from the Shandong Statistical Yearbooks (16).

There were substantial correlations between these three county-level SES variables. Therefore, rather than treating these measures separately, principal component analysis was used to convert these correlated variables into a set of linearly uncorrelated components. Three components were created from the county-level SES variables. Only one of the components had an eigenvalue more than 1 (eigenvalue = 2.00), overall explaining 66.7% of variation in the original SES variables. This component was discretized into three equally sized categories based on its value and named as "SES index". A county with a higher SES index value indicates that, on average, the county had a higher ratio of hospital beds to population and a higher GDP per capita, and the adult residents of that county had more years of formal school education. More information about the generation of SES index can be found in previous paper (18).

Statistical analysis

The 1-, 3-, 5-year cause-specific survival rates were assessed using Kaplan–Meier analysis, with estimates compared between patient subgroups with the log-rank test. The cause-specific survival rate presents the percentage of people who have not died from esophageal cancer in a defined period of time. Therefore, in this study, patients who died from causes other than esophageal cancer were treated as censored cases. Data analysis was conducted using Stata Statistical Software (v15, StataCorp).

The most common model for survival analyses is the Cox regression model or its variants (26). Because our data do not meet the proportion hazards assumption, the Cox model with time varying coefficients was considered (27). However, it does not retain the underlying hierarchical structure of the data. Another variation, the Cox model with mixed effects is appropriate for hierarchical structure data, however it only accounts for two-level data (28), thus is not suitable for the three-level structure data in this study. The multilevel mixed-effects parametric survival model is another option, however, none of the assumed distributions for the hazard function (28): exponential, Weibull, lognormal, loglogistic, or gamma distribution fitted the survival data in this study.

For these reasons, we used a discrete-time multilevel mixed-effects survival model for the survival analysis in this study. The discrete-time multilevel mixed-effects survival model is fitted to an expanded person-period dataset, containing a sequence of binary responses for each individual from each event time (29). This binary response variable was coded as 1 if an individual died during a time interval t (measured in years, time interval = 0–1; 1–2; . . .; 4–5) and 0 otherwise. A three level mixed-effects regression model for binary outcomes was then used to model the probability that the events occurred at a specific discrete-timepoint, conditional on the fact that it had not yet occurred (28). The models were used to examine the potential roles of individual-level and area-level SES factors on survival of esophageal cancer in the Shandong population and the survival difference between the high-mortality cluster and noncluster areas. Because some of the SES covariates presented nonproportional hazards, interactions between time intervals and independent covariates were considered in the model. HRs reflecting the linear combinations of independent covariates and their interactions with each time interval were reported.

Results

Kaplan–Meier survival analysis

Among the final study cohort, the 1-, 3-, and 5-year cause-specific survival rate were 59.6%, 31.9%, and 23.6%, respectively (Table 1). The hazard of dying from esophageal cancer increased in the first 8 months after diagnosis and decreased gradually after, for both male and female (Fig. 1).

Unadjusted cause-specific survival decreased with increasing age ($P < 0.01$). Poorer survival outcomes were also seen for patients who were blue-collar workers ($P < 0.01$), living in rural areas ($P < 0.01$), living in counties with lower SES index ($P < 0.01$), or living in noncluster areas ($P < 0.01$; Table 1; Fig. 2).

Discrete-time survival models with mixed effects

The multilevel model suggested that patients in blue-collar jobs at diagnosis had 1.39 times higher risk of death due to esophageal cancer than those employed in white-collar jobs in the first year after diagnosis (Table 2). The corresponding number was 1.32 in the second year after diagnosis. The differences of esophageal cancer–related death risk between blue- and white-collar patients were not significant after 2 years of diagnosis.

When compared with patients living in urban areas, those living in rural areas had 1.18, 1.22, and 1.17 times higher risk of esophageal cancer–related death in the first, second, and third year postdiagnosis, respectively (Table 2). The differences became nonsignificant after 3 years of diagnosis. It is worth noting that, when we used the county-level classification approach that applied in previous national study (2), rural patients had higher risk of esophageal cancer–related death in the first year after diagnosis (HR, 1.20; 95% CI, 1.02–1.41), but lower risk of esophageal cancer–related death in the fourth and fifth year after diagnosis, with HR as 0.71 (95% CI, 0.56–0.89) and 0.64 (95% CI, 0.46–0.88), respectively. The death risk differences were not significant in the second and third year after diagnosis (results not shown in table).

The survival differences between patients living in middle/low SES index counties and those living in high SES index counties were not significant in the first 2 years of diagnosis (Table 2). However, patients living in middle SES index counties had 3.11 times higher risk of death than those living in high SES index counties in the third year postdiagnosis, and had 5.67 times higher risk of death than those living in high SES index counties in

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Table 1. Cohort description and unadjusted 1-, 3-, and 5-year estimates of cause-specific outcomes for patients with esophageal cancer ages 20+ years in Shandong Province, 2005–2014

	EC patients (*N*)	1-year (%) Survival	1-year (%) 95% CI	3-year (%) Survival	3-year (%) 95% CI	5-year (%) Survival	5-year (%) 95% CI	*P*[a]
All cohort	65425	59.6	59.2–59.9	31.9	31.5–32.3	23.6	23.1–24.0	—
Individual-level variables								
Age								<**0.01**
20–39	313	64.1	58.4–69.2	42.7	36.8–48.4	35.3	29.1–41.5	
40–59	17,623	67.3	66.6–68.0	40.2	39.4–41.0	31.1	30.2–31.9	
60–79	39,755	59.6	59.1–60.1	31.3	30.8–31.8	22.6	22.1–23.2	
80+	7,734	41.2	40.0–42.3	15.2	14.5–16.1	9.2	8.2–10.1	
Sex								=**0.12**
Male	48,589	59.5	58.8–60.3	32.7	31.9–33.5	24.4	23.6–25.3	
Female	16,836	59.6	59.1–60.0	31.6	31.2–32.1	23.2	22.7–23.7	
Occupation								<**0.01**
White-collar	2,721	70.4	68.6–72.1	43.8	41.7–45.8	31.9	29.4–34.3	
Blue-collar	49,875	57.5	57.1–58.0	29.1	28.7–29.6	20.8	20.4–21.3	
Others	3,028	65.0	63.3–66.7	39.3	37.3–41.4	29.6	27.2–32.1	
Unknown	9,801	65.3	64.3–66.2	40.8	39.7–41.9	33.5	32.3–34.6	
Subarea-level variable								
Residency type								<**0.01**
Urban	15,518	64.8	64.0–65.5	39.2	38.4–40.1	29.8	28.8–30.8	
Rural	49,907	57.9	57.5–58.4	29.7	29.3–30.2	21.7	21.3–22.2	
Area-level variables								
Index of SES								<**0.01**
High	903	70.6	67.4–73.5	51.6	47.8–55.3	46.1	41.8–50.3	
Middle	7,259	61.8	60.7–63.0	35.3	34.0–36.5	27.0	25.6–28.5	
Low	57,270	59.1	58.7–59.5	31.2	30.8–31.7	22.9	22.4–23.3	
Geographic type								<**0.01**
Noncluster	42,690	58.3	57.9–58.8	30.8	30.3–31.3	21.2	20.6–21.7	
Cluster	22,735	61.8	61.2–62.5	34.0	33.3–34.6	26.9	26.2–27.6	

NOTE: The *P* value (=0.12) is shown in the last cell of the row for "Sex," which is consistent with other variables.
Abbreviation: EC, esophageal cancer.
[a]*P* value is a comparison of Kaplan–Meier curves from log-rank test.

the fifth year postdiagnosis. The corresponding number for patients living in low SES index counties were 2.64 and 6.47, respectively, compared with those living in high SES index counties.

After adjustment of sex, age, diagnosis period, and SES variables, patients with esophageal cancer living in the high-mortality cluster area had better survival in almost all time intervals, with the risk of dying from esophageal cancer for those living in noncluster areas being 1.26, 1.33, 1.35, 2.23, and 2.14 times higher than for those living in the cluster area in the first, second, third, fourth, and fifth year postdiagnosis (Table 2).

Sensitivity analysis

Because 74% of the missing follow-up cases were diagnosed between 2013 and 2014, we did a sensitivity analysis, which excluded all patients diagnosed between 2013 and 2014. The sensitivity analysis revealed little change in the cause-specific survival rate (Supplementary Table S3).

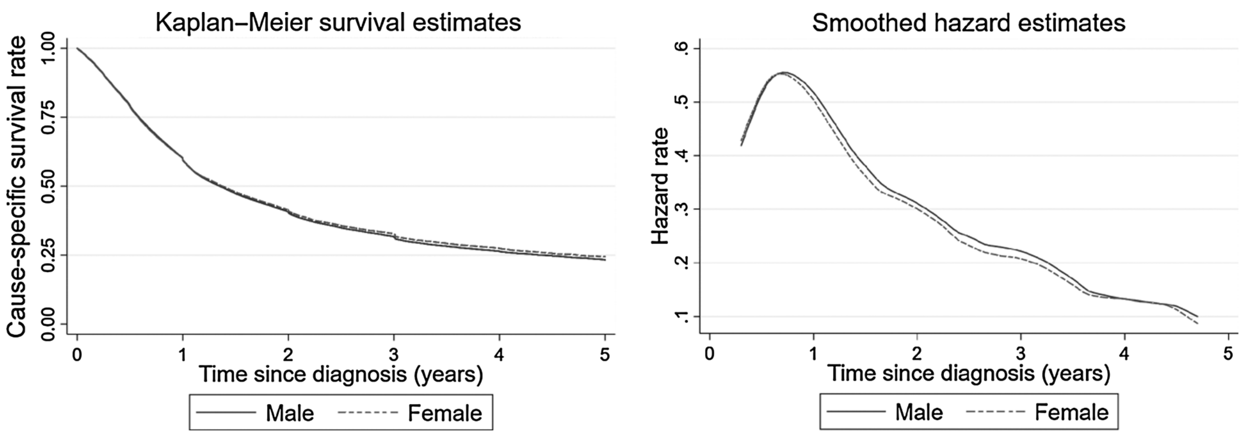

Figure 1.
Cause-specific Kaplan–Meier survival curve (left) and smoothed hazard curve (right) for the patients with esophageal cancer ages 20+ years in Shandong Province, 2005–2014.

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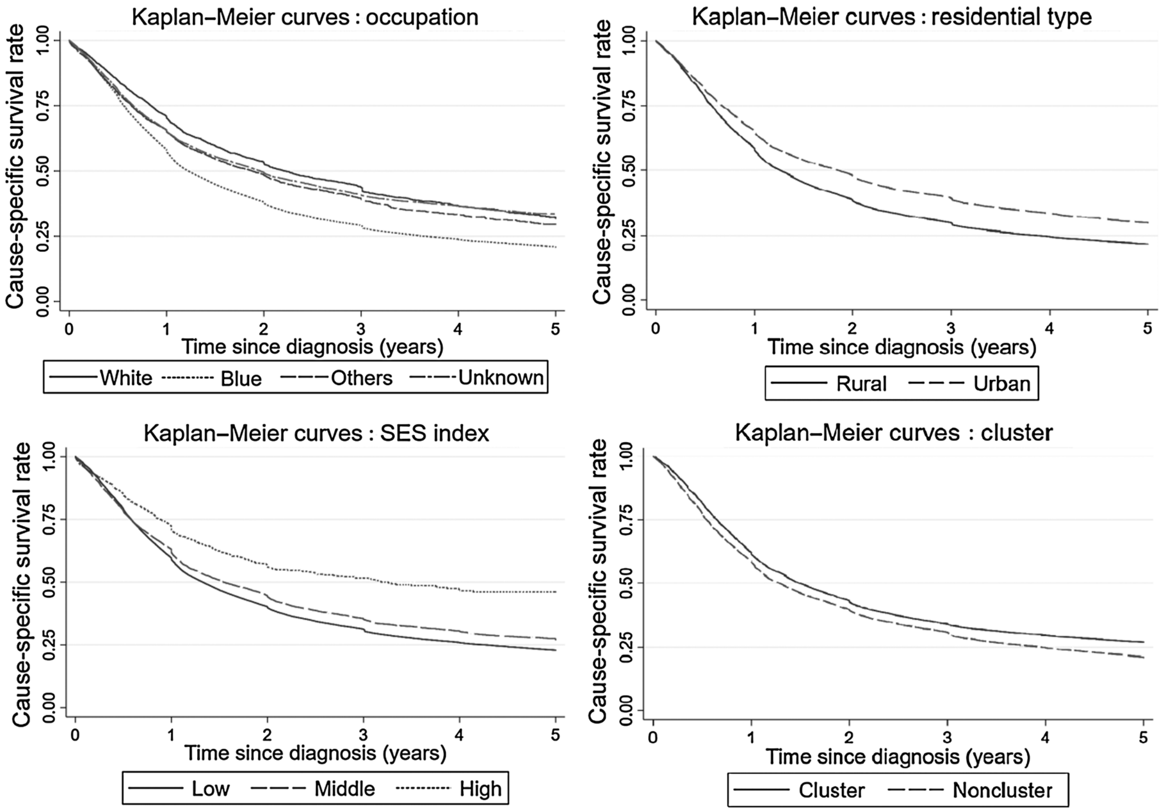

Figure 2.

Cause-specific Kaplan–Meier survival curves for patients with esophageal cancer ages 20+ years in Shandong Province, 2005–2014 by occupation (upper left), residential type (upper right), SES index (lower left), and cluster variable (lower right).

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Table 2. Association between SES factors and cause-specific mortality in patients with esophageal cancer within 5 years postdiagnosis, ages 20+ years in Shandong Province, 2005–2014

	0–1 years after diagnosis		1–2 years after diagnosis		2–3 years after diagnosis		3–4 years after diagnosis		4–5 years after diagnosis	
	HR[a,b] (95% CI)	P[b]	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Individual-level variables										
Occupation										
White-collar[c]	1	–	1	–	1	–	1	–	1	–
Blue-collar	1.39 (1.29–1.50)	<0.01	1.32 (1.20–1.47)	<0.01	1.17 (1.00–1.36)	0.06	0.92 (0.74–1.14)	0.45	0.92 (0.64–1.32)	0.66
Others	1.16 (1.06–1.28)	<0.01	1.10 (0.98–1.25)	0.11	0.97 (0.82–1.15)	0.74	0.77 (0.61–0.96)	0.02	0.77 (0.53–1.10)	0.16
Unknown	1.18 (1.09–1.28)	<0.01	1.13 (1.01–1.26)	0.03	0.99 (0.84–1.17)	0.91	0.78 (0.64–0.98)	0.03	0.78 (0.55–1.12)	0.19
Subcounty-level SES variable										
Residential type										
Urban[c]	1	–	1	–	1	–	1	–	1	–
Rural	1.18 (1.10–1.26)	<0.01	1.22 (1.12–1.32)	<0.01	1.17 (1.06–1.30)	<0.01	1.14 (0.99–1.32)	0.07	0.95 (0.77–1.16)	0.60
County-level SES variables										
SES index										
High[c]	1	–	1	–	1	–	1	–	1	–
Middle	1.41 (0.92–2.15)	0.11	1.53 (0.97–2.41)	0.07	3.11 (1.71–5.67)	<0.01	1.70 (0.84–3.45)	0.14	5.67 (1.29–24.80)	0.02
Low	1.30 (0.86–1.95)	0.21	1.36 (0.88–2.11)	0.17	2.64 (1.47–4.76)	<0.01	1.92 (0.96–3.83)	0.06	6.47 (1.50–27.89)	0.01
Cluster variable										
Cluster[c]	1	–	1	–	1	–	1	–	1	–
Noncluster	1.26 (0.99–1.61)	0.06	1.33 (1.04–1.70)	0.03	1.35 (1.05–1.74)	0.02	2.23 (1.71–2.91)	<0.01	2.14 (1.59–2.88)	<0.01

NOTE: Model included diagnosis period, age group at diagnosis, sex, occupation, residential type, SES index, cluster variable, and interactions between time intervals and the mentioned covariates. Likelihood-ratio tests showed better model fit for the final model when compared with model without interactions.

[a]HR, adjusted hazard ratio.

[b]HRs and *P* values were linear combination between independent covariates and their interactions with each time interval.

[c]Reference group in the mode.

Discussion

This large population-based study is the first to elucidate the influence of SES at three different levels in the population of Shandong, China. We found that the cause-specific survival up to 5 years after diagnosis was independently associated with the patient's occupation and where they live, with better survival for patients doing a white-collar job (individual level), residing in urban area (subcounty-level), living in a county with higher SES index (county-level), or high-mortality cluster area.

The overall 5-year cause-specific survival of esophageal cancer in the Shandong population was 23.6% in the research period (2005–2014). A national study reported a 5-year relative survival of 25.6% in a similar time period (2). The national study is based on data from 17 cancer registries in east China, with one of the registries located in Shandong Province (30). Two other survival analyses based on data from two county-level cancer registries located in east and west China reported 5-year all-cause survival for esophageal cancer as 19.6% in 2002–2014 and 18.6% in 2008–2013, respectively (31, 32). Although the different survival measurements were not directly comparable, results from this study are largely consistent with other Chinese studies at similar period.

The model results suggested that occupation was associated with esophageal cancer survival in the first 2 years after diagnosis, with blue-collar workers having poorer survival compared with white-collar ones. The results are independent of a patient's age, sex, year of diagnosis, and where they live. Studies in European countries such as England, Wales, and Denmark reported a weak relationship between esophageal cancer survival and individual-level SES (11, 12). While the treatment for cancer is largely free for the residents living in these countries (33, 34), the situation is quite different in China. Chinese patients have to pay between 30% and 100% of their medical service costs (35), meaning patients with low individual SES might avoid to seek medical services when their early symptoms appear (36) or could not afford the necessary treatment after diagnosis. This may be one potential reason for the positive association between individual SES and short-term survival of esophageal cancer after diagnosis in the Shandong population.

After the adjustment of occupation and SES index, a large gap in survival still existed between rural and urban patients, with a 17%–22% increased risk among rural patients to die from esophageal cancer within 3 years of diagnosis. This finding is inconsistent with the national study, which reported better survival from esophageal cancer for rural patients (2). Two reasons could partially explain the conflicting results. As mentioned in the Materials and Methods, the national study used more heterogeneous county level approach for residential type classification (2), while we used the subcounty-level approach, the latter of which was consistent with the national standards of urban and rural deviation (24). Our analysis using the county-level approach (similar as the national study) also showed a better survival for rural patients in the fourth and fifth year after diagnosis. Furthermore, the sample size in the national study ($n = 17$ sites) is relatively small, with only three sites classified as urban (30). Therefore the true difference between rural and urban dwellers might have been confounded by the geographic variations between provinces or broad regions. As a unique strength, our study was conducted with a highly homogeneous population using classification that is consistent with the official standard. Therefore, we are quite confident that the pattern we observed with poorer survival in rural patients is likely to be true at least in the Shandong population.

International studies suggested a better survival of esophageal cancer for urban patients when compared with rural ones (37). However, the relationship becomes insignificant after adjusting for cancer treatment and stage at diagnosis (38, 39). The treatment and diagnosis differences could also be one of the reasons for the poorer survival in the rural patients observed in our study. In China, the health insurance systems are different between urban and rural residents, with rural patients usually needing to pay a higher percentage of their medical service costs than urban patients even in the same hospital (35). This may lead to suboptimal treatment among rural patients. In addition, most of the tertiary referral hospitals in China are in urban areas. The different health insurance system leads to longer waiting times for medical investigation and referral for diagnosis for rural patients (35, 40). However, because the data on treatment or stage at diagnosis are not available, this study could not elucidate the potential influential factors behind the poorer survival in rural patients.

Patients living in middle and low SES index counties had much higher risk of death after 3 years of diagnosis than those living in high SES index counties. International studies have also reported poorer survival in patients living in socioeconomically disadvantaged areas for esophageal cancer (5, 7, 9, 41). The SES index applied in this study incorporates GDP per capita, years of school education, and hospital bed to population ratio. Local governments in affluent areas with a high GDP level are more likely to allocate a larger proportion of the total expenditure on health care, which may lead to easier access to health resources and better medical services (42). Our study also supported this, finding a significant correlation between a county's GDP per capita and number of hospital beds to population ratio.

In addition to the relationship between SES factors and esophageal cancer survival found in this study, we also revealed that a patient's occupation and residential type were more associated to the short-term (1–3 years) survival of esophageal cancer, while the county-level SES index was more associated with long-term (3–5 year) survival. Studies related to the association between different SES factors on short- and long-term cancer survival are scarce. Our hypothesis is that, as patients with low individual SES or from rural areas usually cannot afford medical services, they might have their disease diagnosed in later stage and have suboptimal or even no treatment. These could lead to a higher mortality risk within short-term after diagnosis. On the other hand, counties with higher SES index were associated with more expenditure on health care. It is usually related to more up-to-date cancer treatment in those counties. Studies have reported that treatment is a strong predictor for long-term cancer survival in terms of complication and recurrence (43, 44).

After adjustment for age, sex, period of diagnosis, and SES factors, patients living in the high-mortality cluster area had a lower risk of dying from esophageal cancer within 5 years of diagnosis, when compared with the remaining areas of the province. The result suggested that the higher mortality due to esophageal cancer in the cluster area is not because of poorer survival, but rather due to higher incidence, a pattern which has been previously reported in some counties located in the cluster area (45). However, because incidence information is not available at the provincial level, it is difficult to confirm this hypothesis.

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Since 2006, the National Oesophageal Cancer Screening Program for Early Detection and Treatment has been conducted in a few counties located in the high-mortality cluster area. The program provides endoscopy and biopsy for residents to early detect esophageal cancer and its preneoplastic lesions (46). Studies reported that during the program, 87.9% of the diagnosed cases are in early stage (47). Earlier detection leading to more effective treatment of esophageal cancer in the cluster area is likely to at least partially explain for the longer survival times.

This study has several limitations. Because some of the counties just started to reported cancer incident cases, 13.8% of the 2005–2014 registration records did not have follow-up information. However, sensitivity analysis showed that the excluded missing follow-up data have limited influence on the key patterns observed in this study. The other limitation is we did not have cancer treatment and stage information, which are strong indicators for cancer survival outcomes. Therefore, we could not elucidate the association between individual and area-level SES on cancer stage and treatment choices.

Conclusion

Our study provides unique insights into the prognosis of esophageal cancer in a large Chinese population. By elucidating the relative roles of SES factors on survival, the results could guide interventions to reduce disparities in the prognosis of esophageal cancer in China. Finally, we found that the higher mortality rate in the cluster area of Shandong is unlikely to be caused by poorer survival rates but was more likely caused by a higher incidence of esophageal cancer in that area. While it remains crucial to collect more detailed information on diagnoses and treatment patterns, these findings provide important evidence to help tailor public health strategies for this vulnerable group.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: K. Kou, P.D. Baade, J. Sun, Z. Lu, A. Xu, X. Guo
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Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): J. Sun, Z. Lu, Z. Fu, J. Chu, A. Xu, X. Guo
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): K. Kou, S.M. Cramb, J. Sun, X. Guo
Writing, review, and/or revision of the manuscript: K. Kou, P.D. Baade, M. Gatton, S.M. Cramb, J. Sun, Z. Lu, A. Xu, X. Guo
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): J. Sun
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