

Determinants for Aggressive End-of-Life Care for Oral Cancer Patients

A Population-Based Study in an Asian Country

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Abstract: Few studies have addressed the association between oral cancer and end-of-life (EOL) aggressive care using population data. We investigated the relationship between patient demographics, primary physician's specialty, and hospital characteristics of patients who died from oral cancer in Taiwan from 2009 to 2011 and the aggressiveness of their EOL care.

This nationwide population-based, retrospective cohort study identified 5386 patients who died from oral cancer identified from Taiwan's National Register of Deaths Database and collected their claims data from Taiwan's National Health Insurance Research Database. Accepted indicators of aggressiveness of EOL care were examined using a composite measure adapted from Earle et al. Scores ranged from 0 to 6; the higher the score, the more aggressive the EOL care. The impact of each variable on the aggressiveness of EOL care was examined by multivariate analysis using a random-intercept model.

The mean composite score for aggressiveness of EOL care was 2.68 ± 1.37 . Oral cancer patients who were younger, had a higher level of comorbidity or metastasis, belonged to a lower-level individual socioeconomic status, were cared for by nononcologists, had longer postdiagnosis survival times, or resided in urban areas were more likely to receive aggressive care at EOL. Compared with previous studies, oral cancer patients near death in this nationwide study had a far higher utilization rate (>50%) of chemotherapy, emergency room services, and intensive care unit services.

Our findings indicate that oral cancer patients receive extensive

aggressive medical care at EOL. Future research may be needed to examine the effect of the means (indicators) of aggressive treatment on survival, quality of life, and medical costs, especially since current research suggests such care may adversely affect quality of life and important preparation of death in these patients.

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Abbreviations: EOL = end-of-life, ER = emergency room, ICU = intensive care unit, NHI = national health insurance, NHIRD = National Health Insurance Research Database, SES = socioeconomic status.

INTRODUCTION

Oral cancer is 1 of the 10 most common cancers in the world.¹ Its incidence has been rising not only in Asian countries such as Taiwan where betel nut consumption is high but also now in Western countries.^{2,3} Oral cancer makes up for 70% of all head and neck cancers in Taiwanese males, and has been ranked fourth in incidence and mortality in that population since 1995. Treatment of this disease amounted to US\$1195 million in Taiwan in 2004. These expenditures are expected to increase dramatically in this decade, making oral cancer treatment a serious socioeconomic problem for a country that provides national health insurance (NHI) and an important public health issue.

An initial diagnosis of advanced-stage oral cancer carries with it a 35% chance of being cured.⁴ As the disease progresses, there is a concomitant increase in physical distresses and functional challenges. Although there are many different treatment options available to help relieve uncontrolled suffering of oral cancer at end-of-life (EOL), there is a paucity of information regarding the prognosis of this disease, treatment modalities, and the possible complications of medical care.^{5,6} This makes proper EOL treatment decision making very difficult.

Previous studies from around the world have reported increasing aggressiveness in treatment for cancer near EOL, including increases in chemotherapy, hospital stay, intensive care unit (ICU) admission, emergency room (ER) visits, and deaths during acute care hospitalizations.⁷⁻¹⁰ In many instances, not only these treatments do *not* cure disease but they are also performed at high cost and compromise the quality of life of the patient close to death.¹¹ These studies, however, focus on the impact of aggressive EOL treatment for all cancers, not on oral cancer, which is now on the increase outside of Asia.

This study uses the nationwide claims data from Taiwan's National Health Insurance Research Database (NHIRD) for patients who died from oral cancer between 2009 and 2011 to investigate the determinants of aggressive medical care for patients with oral cancer near death. This database provides basic demographic data as well as socioeconomic status (SES),

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disease severity, medical services, hospital characteristics, and hospital stay data.

METHODS

Ethics Statement

This study was approved by the Institutional Review Board of Buddhist Dalin Tzu Chi General Hospital, Taiwan. Review board requirements for written informed consent were waived because all personal identifying information was removed from the data set prior to analysis.

Database

We first accessed the National Register of Deaths Database to identify 5386 patients who died from oral cancer from 2009 to 2011. We then collected individual patient-level data for this study from Taiwan's NHIRD for the years 2009 to 2011. This data set is organized and managed by Taiwan's National Health Research Institutes but collected by Taiwan's NHI program, which has been in place in Taiwan since 1995. The program covers approximately 99% of the residents in Taiwan and has contracts with 97% of the medical providers there.¹² To verify accuracy of diagnosis, Taiwan's Bureau of National Health Insurance randomly reviews the charts of 1 per 100 ambulatory and 1 per 20 inpatient claims and interviews patients.^{13,14} Taiwan's NHI program is a single-payer system with the government as sole insurer and provides universal insurance coverage for comprehensive array of medical services for all of Taiwan's residents. Patients have free access to any medical care provider they choose as long as that provider has a contract with the Bureau of National Health Insurance.

Measurement

Aggressiveness of EOL Care

This study adopted the 6 indicators of aggressiveness of EOL care from Earle et al.^{7,15} These 6 indicators were use of chemotherapy, more than 1 ER visit, more than 1 hospital admission, more than 14 days of hospitalization, an ICU admission, and death in acute care hospital, all within the last month of life. Data for all of these indicators could be collected from Taiwan's NHIRD, which maintains records for all inpatient or outpatient claims for the last month of life. Regardless of whether a patient was enrolled in hospice home care or inpatient hospice services in the last month of life, hospitalization was not counted as aggressive care. Each person who died from oral cancer received a score of 1 point per indicator. With a total of 6 indicators, the composite score for each person ranged from 0 to 6, with higher scores indicating more aggressive EOL care.

Patient Demographics

Patient characteristics included age, gender, postdiagnosis survival time, geographic location, urbanization level of residence, individual SES, cancer metastatic status, and severity of comorbidity. The recoding and definition of SES and urbanization of residence was mentioned in our previous study.¹⁶ Severity of comorbidity was based on the modified Charlson Comorbidity Index Score recorded on the claims database for the last 6 months of each patient's life. The Charlson Comorbidity Index Score is a widely accepted scale used for risk adjustment in administrative claims data sets.¹⁷ Oral cancer metastatic status was identified by International Classification of Diseases, Ninth Revision, codes 196.xx to 199.xx.

Primary Physician's Specialty and the Characteristics of the Primary Hospital

The primary physician's specialty was identified from NHI claims and was dichotomized into oncologist versus other. The hospitals were categorized by hospital level (medical center, regional, or district hospital), caseload volume (high, medium, or low), and hospital spending intensity (high, medium, or low). The hospital caseload volume was sorted by their total patient volume using unique hospital identifiers reported in a previous study.¹⁸ The hospital spending index used in this study was based on the hospital EOL expenditure index, defined as the mean spending of hospitalization of patients in their last 6 months of life, modified from previous literature.¹⁹

Statistical Analysis

All statistical operations were performed using SPSS (version 15; SPSS Inc, Chicago, IL). The impact of each explanatory variable on the aggressiveness of EOL care tool was examined by multivariate analysis using a random-intercept model, which accounts for patient clustering within hospitals and the continuous nature of the composite score for EOL care. A hospital-level random effect can account for possible correlations between EOL care within a hospital's panel because of hospital policies, facilities, or physician compensation mechanisms that are unique to a particular hospital. A 2-tailed value of $P < 0.05$ was considered significant.

RESULTS

A total of 5386 patients who died from oral cancer from 2009 to 2011 were identified in the National Register of Deaths Database. As can be seen in Table 1, which shows a summary of patient characteristics, mean age at death was 57 ± 13 years. The majority (72.5%) of patients who died from oral cancer were between 35 and 64 years old. Most (64%) also had metastatic disease. Among the decedents with oral cancer, almost 30% died within 6 months after diagnosis. In the last month of life, 15.4% of these patients were treated by oncologists.

As can be seen in Figure 1, which shows a line graph depicting distribution of aggressive EOL care indicators over 3 years, the mean composite score for aggressiveness of EOL care was 2.68 ± 1.37 with most oral cancer patients (96.1%) having at least 1 indicator of aggressive EOL care (Table 2). In the majority of these patients, there was an increase in frequency of ER visits and ICU admissions in the last month of life in 2010 and 2011 compared with that in 2009. Besides, only 644 (12%) patients enrolled in hospice services in the last month of life.

Compared with the composite aggressive EOL care scores of 2009, those of 2010 and 2011 were not significantly higher ($P = 0.150$ and 0.626 , respectively), after controlling for other variables (Table 3). EOL care was found to be less aggressive for oral cancer patients who belonged to a high SES, who were older than 85 years, who resided in rural areas, who were primarily cared for by oncologists, and who had postdiagnosis survival times shorter than 6 months. It was found to be significantly more aggressive for those with higher levels of comorbidity and disease with metastasis (both $P < 0.001$). Aggressiveness of EOL care was not found to be influenced by gender, geographic region, or hospital characteristics, which included hospital level, hospital spending intensity, and caseload volume.

TABLE 1. Baseline Characteristics

Parameter	Total		Year		2010		2011	
	No.	%	No.	%	No.	%	No.	%
Total	5386	100	1369	25.4	1808	33.6	2209	41.0
Socioeconomic status								
High	1418	26.3	355	25.9	448	24.8	615	27.8
Medium	2244	41.7	551	40.2	761	42.1	932	42.2
Low	1724	32.0	463	33.8	599	33.1	662	30.0
Hospital spending index								
High	1318	24.5	345	25.2	449	24.8	524	23.7
Medium	3390	62.9	853	62.3	1118	61.8	1419	64.2
Low	678	12.6	171	12.5	241	13.2	266	12.1
Gender								
Male	5033	93.4	1281	93.6	1670	92.4	2082	94.3
Female	353	6.6	88	6.4	138	7.6	127	5.7
Mean age, years (±SD)	57 ± 13		57 ± 13		57 ± 13		56 ± 13	
Age group, years								
18–34	99	1.8	36	2.6	32	1.8	31	1.4
35–44	882	16.4	238	17.4	295	16.3	349	15.8
45–54	1753	32.5	469	34.3	574	31.7	710	32.1
55–64	1271	23.6	280	20.5	444	24.6	547	24.8
65–74	784	14.6	195	14.2	263	14.5	326	14.8
75–84	459	8.5	113	8.3	148	8.2	198	9.0
≥85	138	2.6	38	2.8	52	2.9	48	2.2
CCIS								
0 or 1	1907	35.4	479	35.0	665	36.8	763	34.5
2	1038	19.3	283	20.7	333	18.4	422	19.1
3	398	7.4	102	7.5	135	7.5	161	7.3
4	2043	37.9	505	36.9	675	37.3	863	39.1
Cancer group								
Without metastasis	1941	36.0	499	36.4	662	36.6	780	35.3
With metastasis	3445	64.0	870	63.6	1146	63.4	1429	64.7
Postdiagnosis survival, mo								
≤6	1499	27.8	447	32.7	504	27.9	548	24.8
7–12	1683	31.2	567	41.4	544	30.1	572	25.9
13–24	1650	30.6	355	25.9	602	33.3	693	31.4
>25	554	10.3	0	0.0	158	8.7	396	17.9
Primary physician's specialty								
Oncologist	831	15.4	213	15.6	284	15.7	334	15.1
Other	4555	84.6	1156	84.4	1524	84.3	1875	84.9
Hospital characteristics								
Medical center	3828	71.1	975	71.2	1291	71.4	1562	70.7
Regional	1461	27.1	364	26.6	486	26.9	611	27.7
District	97	1.8	30	2.2	31	1.7	36	1.6
Caseload group								
High	1255	23.3	278	20.3	423	23.4	554	25.1
Medium	2132	39.6	566	41.3	719	39.8	847	38.3
Low	1999	37.1	525	38.3	666	36.8	808	36.6
Urbanization								
Urban	1244	23.1	312	22.8	406	22.5	526	23.8
Suburban	2361	43.8	614	44.9	787	43.5	960	43.5
Rural	1781	33.1	443	32.4	615	34.0	723	32.7
Geographic Region								
Northern	2351	43.7	609	44.5	767	42.5	975	44.2
Central	1042	19.4	274	20.0	356	19.7	412	18.7
Southern	1698	31.5	419	30.6	571	31.6	708	32.1
Eastern	291	5.4	67	4.9	111	6.1	113	5.1

CCIS = Charlson Comorbidity Index Score, SD = standard deviation.

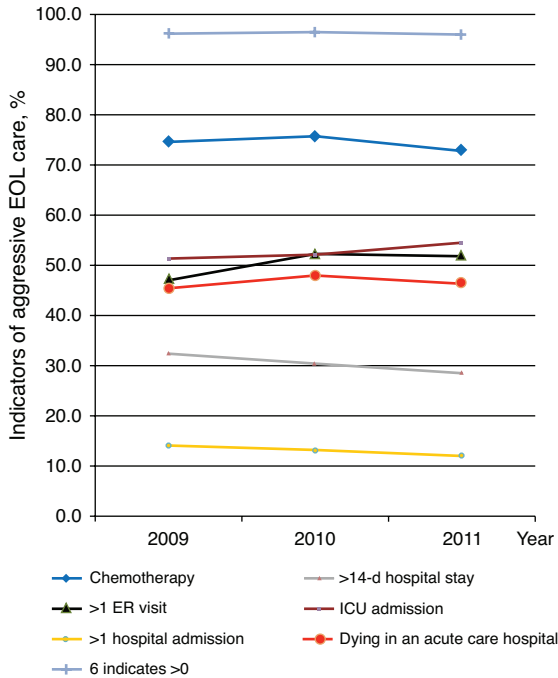


FIGURE 1. Trends for the 6 indicators of aggressive EOL care for Taiwanese patients who died from oral cancer from 2009 to 2011. EOL=end-of-life, ER=emergency room, ICU=intensive care unit.

DISCUSSION

In this study tapping Taiwan’s NHIRD claims records for patients who died from oral cancer between 2009 and 2011, it was found that 96.1% of those patients who died from this disease between 2009 and 2011 had at least 1 of the 6 indicators of aggressive care (forms of aggressive treatment) near the EOL used by Earle et al,^{7,15} and that composite aggressive EOL care scores for 2010 and 2011 were not significantly higher than those found in 2009 ($P = 0.150$ and 0.626 , respectively). There was a high utilization rate in chemotherapy, ER visits, and ICU

admissions in the last month of life in more than 50% of these oral cancer patients.

The finding of tendency toward aggressiveness of care at EOL is consistent with those of earlier studies investigating aggressive EOL care and cancer death, although none studied oral cancer specifically.^{7–10} Those studies reported this trend to be increasing over time, but not seen in our result. Similar to previous reports,^{7–10,20,21} we found that patients who were elderly (≥ 85 years), who had lower level of comorbidity indices, who had no distant metastasis, or who were living in the rural area were less likely to receive aggressive EOL treatment. Our findings differ from previous findings first with regard to the impact of variables on aggressiveness of EOL care in our study population. Earle et al,^{7,8} Tang et al,⁹ Ho et al,¹⁰ Saito et al,²⁰ and Warren et al²² found that cancer patients who were male gender, who were primarily cared for by oncologists, who had higher-level individual SES, who had shorter post-diagnosis survival time, or who were treated in teaching hospitals were more likely to have 1 or more indicators of aggressive EOL care (eg, chemotherapy, ICU utilization, ER visits). Residence region was also a significant independent predictor of intensive EOL care in those studies. However, in our study of oral cancer patients, aggressiveness of EOL care was not influenced by sex, hospital teaching level, and residence area, and patients who had higher-level individual SES, who had shorter postdiagnosis survival times (< 6 months), or who were treated by oncologists had lower composite aggressive EOL care scores. The reason may be due to poor prognosis of advanced-stage oral cancer that has not shown any significant improvement over the past few decades.²³ Diseases have generally been treated much less aggressively if they were considered highly fatal.²⁴ Previous studies did not investigate the relation between hospital spending and hospital caseload volume. We did, but found no significant difference with regard to the influence of these variables and aggressiveness of EOL care. Tang et al, studying a cohort of patients who died from cancer in Taiwan from 2001 to 2006, found that from 10% to 20% of cancer patients near death received chemotherapy, were admitted to ICUs, or had emergency department visits.⁹ However, we found that more than 50% of oral cancer patients near death were admitted to ICUs and had emergency department visits and almost 70% received chemotherapy in the last month

TABLE 2. Trends in Aggressive End-of-Life Care for Taiwanese Patients Who Died From Oral Cancer From 2009 to 2011

Composite Score*	Decedents							
	Total		2009		2010		2011	
	n	%	n	%	n	%	n	%
0	212	3.9	54	3.9	66	3.7	92	4.2
1	878	16.3	250	18.3	274	15.2	354	16.0
2	1450	26.9	357	26.1	500	27.7	593	26.8
3	1374	25.5	336	24.5	458	25.3	580	26.3
4	934	17.3	226	16.5	327	18.1	381	17.2
5	415	7.7	116	8.5	142	7.9	157	7.1
6	123	2.3	30	2.2	41	2.3	52	2.4
Average								
Mean	2.68		2.66		2.72		2.67	
SD	1.37		1.39		1.35		1.36	

SD = standard deviation.

* Composite score measured aggressiveness of end-of-life care (scores range from 0 to 6).

TABLE 3. Determinants of Aggressive End-of-Life Care for Taiwanese Patients Who Died From Oral Cancer From 2009 to 2011 by Multivariate Analysis Using a Random-Intercept Mode

Parameter	Estimate (95% CI)	P Value
Intercept	2.441 (2.084–2.798)	<0.001
Socioeconomic status		
Low	Reference	
Medium	−0.090 (−0.176 to −0.004)	0.039
High	−0.121 (−0.216 to −0.026)	0.012
Hospital spending index		
Low	Reference	
Medium	−0.213 (−0.367 to −0.059)	0.007
High	0.008 (−0.232 to 0.249)	0.944
Gender		
Male	Reference	
Female	0.075 (−0.073 to 0.224)	0.319
Age group, years		
<35	Reference	
35–44	−0.108 (−0.384 to 0.167)	0.442
45–54	−0.086 (−0.356 to 0.182)	0.528
55–64	−0.078 (−0.352 to 0.194)	0.571
65–74	−0.225 (−0.505 to 0.055)	0.116
75–84	−0.363 (−0.655 to −0.071)	0.015
≥85	−0.495 (−0.844 to −0.146)	0.005
Charlson Comorbidity Index Score		
0 or 1	Reference	
2	0.432 (0.331–0.534)	<0.001
3	0.630 (0.485–0.775)	<0.001
≥4	0.464 (0.378–0.550)	<0.001
Cancer group		
Without metastasis	Reference	
With metastasis	0.203 (0.122–0.285)	<0.001
Postdiagnosis survival, mo		
0–6	Reference	
6.01–12	0.168 (0.074–0.262)	<0.001
12.01–24	0.116 (0.020–0.213)	0.018
>24	0.074 (−0.060 to 0.208)	0.280
Primary physician’s specialty		
Other	Reference	
Oncologist	−0.108 (−0.212 to −0.005)	0.039
Hospital characteristics		
Medical center	Reference	
Regional	−0.094 (−0.248 to 0.058)	0.216
District	−0.086 (−0.411 to 0.237)	0.599
Caseload group		
High	Reference	
Medium	0.193 (0.013–0.374)	0.037
Low	0.172 (−0.035 to 0.379)	0.098
Urbanization		
Urban	Reference	
Suburban	−0.081 (−0.181 to 0.033)	0.107
Rural	−0.146 (−0.276 to −0.024)	0.014
Geographic region		
Northern	Reference	
Central	0.136 (0.014–0.259)	0.029
Southern	0.020 (−0.085 to 0.125)	0.704
Eastern	0.041 (−0.152 to 0.236)	0.671
Year		
2009	Reference	
2010	0.069 (−0.025 to 0.163)	0.150
2011	0.023 (−0.069 to 0.116)	0.626

CI = confidence interval.

of life. Our results suggest that physicians may have more aggressive attitude toward EOL treatment and provide more intensive treatment for oral cancer patients than for other cancer patients.

More than half of the oral cancer patients we studied had distant metastasis near death. Platinum-based chemotherapy in combination with cetuximab and taxane has been found to improve survival of head and neck cancer patients with distant metastasis.^{25–28} Therefore, it is not surprising that the oral cancer patients in our study had a higher rate of chemotherapy (>70%), although current salvage chemotherapy regimens may prolong life by a matter of months only and have response rates below 50%. Furthermore, platinum- or taxane-based chemotherapy was associated with significant comorbidity, including pancytopenia, nausea, vomiting, stomatitis, and renal toxicity.²⁹ Oral surgeons may fear that they have not done enough in terms of surgery, chemotherapy, or radiotherapy, and may not pay as much attention to the possibility that they have done too much and adversely affected patients' quality of life. Although symptoms related to oral cancer progression may require acute care utilization, the adverse effects of chemotherapy would result in increased numbers of ER visits, ICU admissions, and cases of unexpected toxic complications, which obviously affect quality of life and interfere with preparation for death.³⁰

Physicians tend to overestimate survival time for terminal cancer patients.³¹ They may also feel more comfortable suggesting alternate aggressive treatment goals rather than bringing up the topic of impending death, breaking bad news, and suggesting palliative care.⁶ Shifting to third- or fourth-line chemotherapy may be an easier topic to discuss than hospice care. Avoiding the topic or withholding detailed prognostic information can lead to patient mistrust of the health care system and medical profession, inappropriate use of life-sustaining medical treatments, increased medical complications, and long hospital stays.³² It seems as though physicians give the least honest figures to those with the worst prognoses, often creating unrealistic expectations regarding the potential success of aggressive treatment and interfering with their patients' rights to autonomy and self-determination.³³ A positive association has been found between early EOL discussions and decision to accept less aggressive care.³⁴

However, it is not all in the hands of the physicians, since even after the most frank communications regarding impending death, the patients, themselves, may hold unrealistic expectations and decide to continue chemotherapy.⁵ They may feel that doing something is better than doing nothing. Patients may also associate "palliative care" or "hospice care" with abandonment, an unpleasant emotion that many would prefer to avoid. Avoidance of this emotion can be achieved by distracting themselves with further treatments. Chen et al proposed exploring the subtypes of aggressive EOL care and the potential care quality problems could be better understood in each subtype.³⁵ They classified patients who died from cancer into 3 subgroups based on the usage of aggressive EOL care, such as "not aggressive," "intent to sustain life," and "symptom crisis" group. Thirty-three percent patients who died from cancer were in the "intent to sustain life" subgroup, which was less likely to have metastatic disease and to receive hospice care in the EOL, but more likely to be cared for by nonmedical oncologists, to die within 2 months after diagnosis, and to die in hospital. Besides, the authors also found that the proportions of chemotherapy were similar among 3 subgroups. Chemotherapy for the terminally ill cancer patients was regarded as curative treatment rather than palliative treatment.

Policy Implications

Taiwan's health system is closely intertwined with its NHI program, which covers the health care of almost all of its residents. This universal health insurance program is indeed very costly and takes up much of the nation's resources. Therefore, the problem of unnecessary or unrealistic aggressive treatment is also relevant. Increased aggressiveness translates into great economic burden.^{36,37} In our study, only 12% of oral cancer patients enrolled in hospice services in the last month of life. The more time spent on aggressive EOL care, the less time spent on hospice care. The shorter the time spent in hospice care, the less opportunity for realizing EOL care goals of life closure, comfortable dying, and effective grieving.³⁸ Hospices provide comprehensive, high-quality care that eases oral cancer patients' symptoms and prepares individuals and families for death. In a study of lung cancer patients with metastatic disease, Temel et al suggest that early palliative care can lead to significant improvements in quality of life, mood, and as much as 2 extra months of survival.³⁹ Therefore, clinical and health policies might reduce focus on aggressive care when it will not benefit patients in favor of a more humanistic focus on patient comfort as well as more economic hospice care.

In fact, many terminally ill patients prefer home care, because they can be surrounded by their loved ones and minimize costs.⁴⁰ There are, however, substantial disparities in access to hospice services.⁴¹ Tang et al have reported that less than one-third of patients who die from cancer receive hospice care at home in Taiwan.⁴² Therefore, it might be wise for the relevant authorities to encourage equanimity in availability of hospice care and provide more support for the training of hospice care providers.

Limitations of the Study

This study has several limitations. One limitation is that the diagnosis of cancer and any comorbidity was completely dependent on International Classification of Diseases codes. There might have been some misclassification, although Taiwan's Bureau of National Health Insurance randomly reviews the chart and interviews patients in order to verify diagnostic accuracy.^{13,14} Another limitation was that we could not use the claims database to evaluate satisfaction and quality of life in oral cancer patients. Still another limitation is the lack of detailed information about hospitalizations for diagnostic workup and chemotherapy for reducing symptoms among oral cancer patients in the last month of life. It would be overestimated if those hospitalizations and chemotherapy were considered as aggressive treatment at the EOL. However, given the robustness of the evidence and statistical analysis in this study, these limitations are unlikely to compromise our results.

CONCLUSION

In summary, this study found that oral cancer patients who were younger in age, who had more comorbidity or metastasis, who belonged to a lower-level individual SES, who were primarily cared for by nononcologists, who had longer post-diagnosis survival times, or who resided in urban areas were more likely to receive more aggressive care at EOL. Oral cancer patients near death were also observed to have a far higher utilization rate of chemotherapy, ER services, and ICU services than other cancer patients near death. Future research may be needed to examine the effect of these 3 indicators on survival, quality of life, and medical costs.

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