Effects of income and residential area on survival of patients with head and neck cancers following radiotherapy: Working age individuals in Taiwan

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Objectives: 5-year survival rate of head and neck cancer (HNC) after radiotherapy (RT) varies widely from 35% to 89%. Many studies have addressed the effect of socioeconomic status and urban dwelling on survival of HNC, but a limited number of studies have focused on the survival rate of HNC patients after RT. Materials and methods: During the period of 2000–2013, 40985 working age individuals (20< age < 65 years) with HNC patients treated with RT were included in this study from a registry of patients with catastrophic illnesses maintained by the Taiwan National Health Insurance Research Database (NHIRD). Results: The cumulative survival rate of HNC following RT in Taiwan was 53.2% (mean follow-up period, 3.75 ± 3.31 years). The combined effects of income and geographic effect on cumulative survival rates were as follows: high income group >medium income group > low income group and northern > central > southern > eastern Taiwan. Patients with moderate income levels had a 36.9% higher risk of mortality ascompared with patients with high income levels (hazard ratio (HR) = 1.369; p < 0.001). Patients with low income levels had a 51.4% greater risk of mortality than patients with high income levels (HR = 1.514, p < 0.001). Conclusion: In Taiwan, income and residential area significantly affected the survival rate of HNC patients receiving RT. The highest income level group had the best survival rate, regardless of the geographic area. The difference in survival between the low and high income groups was still pronounced in more deprived areas.

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INTRODUCTION

Globally, approximately 670,000 new diagnoses of head and neck cancer (HNC) and 350,000 HNC-related deaths are reported every year (Ray-Chaudhuri et al., 2013). HNC is the sixth most common cancer in Taiwan and the fourth most common among Taiwanese men (Chang et al., 2017a). Radiotherapy (RT) can effectively alleviate HNC (Chu et al., 2016; Reeve et al., 2013; Wu et al., 2016); however, adherence to RT is difficult for patients with severe toxicity associated with RT (Thomas et al., 2017), such as mucositis, taste disturbance, xerostomia, opportunistic infection, trismus, radiation caries, osteonecrosis of the jaw, and progressive periodontal destruction (Cabrera et al., 2013; Kuo et al., 2016c). These comorbidities impair chewing, swallowing, and speaking function.

The post-RT 5-year survival rate of HNC patients varies widely—from 35% to 89% (Hutcheson et al., 2014; Iyer et al., 2015; Langius et al., 2013; Lassig et al., 2012); however, this large variation may result from differences in study designs and inclusion criteria. Many factors affect the survival of HNC patients after RT, including age (Chang et al., 2013; Unal et al., 2015), sex (Olsen et al., 2015; Osazuwa-Peters et al., 2016), race (Osazuwa-Peters et al., 2016), personal habits (e.g., smoking status, alcohol consumption, betel nut chewing) (Chang et al., 2017a), primary tumor site, tumor–node–metastasis stage (Kreppel et al., 2016), human papillomavirus status (Chu et al., 2016), therapy type (Selzer et al., 2015), nutritional status (Chang et al., 2017a), psychiatric disorders (Unal et al., 2015), urbanization (Chang et al., 2013), education (Kjaer et al., 2013), individual and neighborhood socioeconomic status (SES), and geographical area (Chang et al., 2013; Chu et al., 2016; Kjaer et al., 2013; Wu et al., 2016).

Many studies have found that a lower SES is associated with a lower survival rate among HNC patients (Choi et al., 2016; Chu et al., 2016; Olsen et al., 2015; Osazuwa-Peters et al., 2016; Wu et al., 2016). Other studies have revealed that neighborhood SES, geographical area, area-level

56   socioeconomic position (SEP), and urban dwelling, all influence HNC patient survival (Chu et al.,

57   2011; Hagedoorn et al., 2016; Kuo et al., 2016a; Wong et al., 2017). In general, lower

58   neighborhood SES and rural residence are associated with lower survival rate among HNC

59   patients. However, few studies have focused on post-RT survival rate (Kuo et al., 2016a).

60   Prediction of post-RT survival is fundamental for treatment planning by oral reconstruction

61   dentists. Therefore, this study investigated the effects of SES (determined by income) and

62   residential area on post-RT survival among working-age patients with HNC in Taiwan.

63

64   **MATERIALS & METHODS**

65   **Data source and study cohort**

66   Taiwan's National Health Insurance (NHI) program was established in 1995. With 23 million

67   enrollees, it currently covers more than 99% of the Taiwan population. The data from Taiwan's

68   NHI Research Database (NHIRD) are generally reliable and accurate (Chang et al., 2017b). We

69   identified 66,626 patients with HNC who received RT during 2000–2013 from the registry of

70   patients with catastrophic illnesses in the NHIRD. Of them, those with a prior history of cancer

71   ($n = 3131$), incomplete data ($n = 43$), RT procedure codes 36012B or 36011B < 100 times in 75

72   days (since RT commenced; $n = 13,809$), age $\geq$ 65 years ($n = 8,492$), and age $\leq$ 20 years ($n =$

73   166) were excluded (Kuo et al., 2016c). Finally, 40,985 patients who received RT for HNC were

74   included. The study was approved by Kaohsiung Veterans General Hospital (VGHKS15-EM10-

75   02).

76   Applicable International Classification of Diseases, Ninth Revision, Clinical Modification

77   (ICD-9-CM) codes specific to HNC were adopted, namely malignant neoplasms of the lip (ICD-

78   9-CM 140), tongue (ICD-9-CM 141), major salivary glands (ICD-9-CM 142), gums (ICD-9-CM

79   143), mouth (ICD-9-CM 144), other and unspecified parts of the mouth (ICD-9-CM 145),

80   oropharynx (ICD-9-CM 146), nasopharynx (ICD-9-CM 147), hypopharynx (ICD-9-CM 148),

81   other and ill-defined sites within the lip (ICD-9-CM 149), and larynx (ICD-9-CM 161). In addition,

82   RT procedure codes (36012B or 36011B), specific for Taiwan, were included

83

84   **Survival analysis**

85   The start point for survival analysis was the index day, defined as the first day of RT, not the first

86   day of diagnosis establishment. The endpoint of survival analysis was the day of death. For patients

87   who survived until the end of the observation period, December 31, 2013 was considered the

88   endpoint.

89

90   **Income and geographical area**

91   The NHI premium depends on the income of the patients. Thus, although the NHIRD does not

92   record patients' education level, it records their income. We used this to represent the income

93   factor in our design. We categorized monthly income as follows: low, ≤US$547 (≤NT$17,500);

94   moderate, US$547–781 (NT$17,500–NT$25,000); and high, ≥US$781 (≥NT$25,001; the US$–

95   NT$ conversion is based on an average conversion rate of NT$32 to US$1 for 2015–2016). The

96   geographical area was classified as Northern, Central, Southern, and Eastern (including

97   the offshore island group) Taiwan (Figure 1) (Hung et al., 2015).

98

99   **Other variables**

100 Other variables included the date of RT administration (before or after January 1, 2009), tumor

101 origin [oral (ICD-9-CM 140–145) or non-oral (ICD-9-CM 146-149,161)] (Kuo et al., 2016b),

102 use in combination with conventional chemotherapy (cisplatin or 5- fluorouracil; yes or no),

103 mandibulectomy or maxillectomy (yes or no), and excision of HNC malignant tumor within 3

104   months from the index day (yes or no). In patients with HNC of oral origin, the malignant

105   neoplasm sites were the lips, tongue, major salivary glands, gums, mouth floor, and other

106   unspecified parts of the mouth, whereas they were the oropharynx, nasopharynx, hypopharynx,

107   unspecified pharynx, and larynx in patients with HNC of non-oral origin (Kuo et al., 2016b).

108   Volumetric-modulated arc therapy (VMAT) was introduced in 2009 in Taiwan; the cutoff point

109   in this study was also 2009.

110

111   **Statistical analyses**

112   All statistical analyses were performed on SPSS (version 20; SPSS Inc., Chicago, IL, USA). The

113   Pearson chi-square test was used for analyzing categorical variables (sex, geographic region of

114   residence, tumor origin, surgery, chemotherapy, and timing of RT), whereas one-way analysis of

115   variance was employed for the continuous variable (age). The chi-square test of homogeneity was

116   used for comparing survival rates until the end of the observation period between income levels

117   and geographical areas. The Z-test with Bonferroni adjustment was used for post hoc comparisons

118   between groups. The Kaplan–Meier method was used for survival analysis with variables limited

119   to income levels and geographical areas only, whereas differences in the survival curves were

120   identified using the log-rank test. A Cox regression model was adjusted for baseline covariates.

121

122   **RESULTS**

123   **Demographic data and clinical characteristics**

124   In total, 40,985 working-age HNC patients treated with RT (mean age, 49.23 ± 8.66 years; age

125   range, 20.01–64.99 years) were included, and the overall survival rate was 53.2% (mean follow-

126   up period, 3.75 ± 3.31 years; Table 1) until December 31, 2013 (end of the observation period).

127   The age range of the study cohort was limited to 20–65 years because the mandatory retirement

128   age by law in Taiwan is 65 years. Low- and high-income HNC patients had a higher and lower

129   proportion of tumors with oral origin, respectively (Table 1). As shown in Figure 2, the effects of

130   income and geographical area on the cumulative survival rates were in the following orders: high

131   > moderate > low and Northern > Central > Southern > Eastern, respectively. Figure 3A, 3B, and

132   3C depicts Kaplan–Meier plots for overall survival, survival curves according to different

133   geographical areas, and survival curves according to income levels, respectively. Figure 4

134   illustrates a Kaplan–Meier plot of survival of patients with HNC undergoing RT based on

135   geographical area and income. Median survival in years was longest and shortest among patients

136   residing in Northern and Eastern Taiwan, respectively (Northern > Central > Southern > Eastern;

137   Table 2). Median survival was longer in the high-income group than it was in the low- and

138   moderate-income groups. Significant differences were noted in the survival curves according to

139   the geographical area (Table 3).

140

141   **Univariate survival analysis**

142   As shown in Table 2 and Figure 2, among the adult HNC patients ($20 <$ aged < 65 years) residing

143   in different geographical areas, survival was longer among the high-income group than among the

144   low-income group ($p < 0.05$).

145

146   **Cox proportional hazard model**

147   Results of the multivariate Cox proportional hazard model for the mortality of HNC patients

148   receiving RT showed that residential area, income, sex, tumor origin, year of RT administration

149   (before or after 2009), use of tumor excision surgery, and use of combined chemotherapy were

150   associated with survival (Table 4).

151   Being male was most significantly associated with reduced post-RT survival of HNC patients

152   [hazard ratio (HR) = 2.049, 95% confidence interval (CI) = 1.943–2.162, $p < 0.001$]. This was

153   followed by oral origin (HR = 1.660, 95% CI = 1.609–1.712); lower income level (HR = 1.514,

154   95% CI = 1.458–1.572); conventional chemotherapy (HR = 1.504, 95% CI = 1.452–1.558);

155   residential area in Eastern Taiwan (HR = 1.454, 95% CI = 1.362–1.552); timing of RT,

156   mandibulectomy, or maxillectomy (HR = 1.215, 95% CI = 1.137–1.299,); and no tumor excision

157   surgery (HR = 1.181, 95% CI = 1.120–1.246; all $p < 0.001$; Table 4).

158   Patients with moderate income had a 36.9% higher risk of mortality than did those with high

159   income (HR = 1.369; 95% CI = 1.320–1.420, $p < 0.001$). Patients with low income had a 51.4%

160   greater risk of mortality than did those with high income (HR = 1.514, 95% CI = 1.458–1.572, p

161   < 0.001). Patients residing in Central Taiwan had a 12.8% greater risk of mortality than did those

162   residing in Northern Taiwan (HR = 1.128, 95% CI = 1.087–1.171, $p < 0.001$). Patients residing in

163   Southern Taiwan had a 40.2% greater risk of mortality than did those residing in Northern Taiwan

164   (HR = 1.402, 95% CI = 1.355–1.451, $p < 0.001$). Patients residing in Eastern Taiwan had a 45.4%

165   greater risk of mortality than did those residing in Northern Taiwan (HR = 1.454, 95% CI = 1.362–

166   1.552, $p < 0.001$).

167   Men had a 104.9% greater risk of mortality than did women (HR = 2.049, 95% CI = 1.943–

168   2.162, $p < 0.001$). Tumor with oral origins were associated with a 66.0% greater risk of mortality

169   (HR = 1.660, 95% CI =1.609–1.712, $p < 0.001$) than were tumors with non-oral origins. The use

170   of combined chemotherapy was associated with a 50.4% greater risk of mortality (HR = 1.504,

171   95% CI = 1.452–1.558, $p < 0.001$) than was the use of no chemotherapy.

172

173   **DISCUSSION**

174   According to the Surveillance, Epidemiology, and End Results database, the average diagnosis age

175   of laryngeal, oral cavity, and pharyngeal cancer is 62 years. Alvarenga Lde et al. (2008)

176   demonstrated that the average diagnosis age for HNC is 62 years in Brazil. However, we noted

177   that the average diagnosis age of HNC in Taiwan is 51.84 years (Kuo et al., 2016c)—much lower

178   than that reported previously.

179   Individuals from the working-age group (20–65 years) provide the main source of family

180   income and care; thus, any serious illness such as HNC can have a negative impact on their family,

181   society, and country. The incidence of HNC is high in Taiwan. Most HNC patients are men

182   (91.3%) and aged 40–60 years (56.0%) (Hsu et al., 2017; Hwang et al., 2015). Taiwan has the

183   highest oral cancer incidence worldwide. Among younger and male patients, oral and

184   oropharyngeal cancers are more prevalent than hypopharyngeal and laryngeal cancers (Hsu et al.,

185   2017). We focused on the survival of HNC patients who received a complete course of RT.

186   Therefore, patients who received RT at a total dosage < 60 Gy in 75 days were excluded according

187   to our previous protocol (Kuo et al., 2016c). Schwam et al. (2015) reported that the 3-year survival

188   rate of HNC patients after adjuvant radiotherapy was 62.8%—higher than the survival rate of HNC

189   patients who received a complete course of RT in the present study.

190   In general, HNC patients with lower incomes have lower survival rates than those with

191   higher incomes (Gupta et al., 2018; Subramanian & Chen, 2013). Here, HNC patients with high

192   income residing in Northern Taiwan had the highest overall survival rate, whereas those with

193   low income residing in Eastern Taiwan had the lowest overall survival rate (Figure 2). Income

194   had a significant effect on the survival of HNC treated with RT, with the best survival rate being

195   associated with the highest income, regardless of the area of residence. Both income and

196   geographical area have been separately linked to the survival rate of HNC patients treated with

197   RT (Chu et al., 2016; Olsen et al., 2015). According to data published by the Taiwan

198   government, life expectancy, concentration of medical facilities, and accessibility to medical

199   resources are best in Northern Taiwan, followed by Central, Southern, and Eastern Taiwan (Kuo

200   et al., 2016a). Because of worse transport infrastructure and a low density of medical resources,

201   Eastern Taiwan is a medically deprived area. In the present study, regardless of residential area,

202   income was significantly associated with median survival years and curves (Tables 2, Figure 4).

203   Although the overall survival rate of patients residing in Eastern Taiwan was lower than that in

204   other regions, the survival rate of the highest income group in Eastern Taiwan was even greater

205   than that of the highest income group in Southern Taiwan (Figure 2). However, no significant

206   difference in the overall survival rate was noted among patients with the highest income in

207   Eastern, Central, and Southern Taiwan (Figure 2), probably because patients with higher income

208   have a greater ability to cross regions and access better medical treatment and facilities (Yi-Chen

209   & Chin-Hung, 2010). Our results also demonstrated that a higher income was associated with a

210   higher survival rate in each regional area, and the differences in the survival curves and median

211   survival years between the medium- and low-income groups were smaller than the differences

212   between the high- and low-income groups or between the high- and moderate-income groups

213   (Figure 4, Table 2). We analyzed the interaction effect between income level and residential

214   area, income, and surgery on post-RT mortality. Some interactions were discovered, and the

215   trend was comparable to the original model—a more deprived residential area and lower income

216   were associated with higher post-RT mortality. Interaction effects between income level and

217   surgical treatment were also noted. Among patients without tumor excision surgery, lower

218   income was associated with higher mortality HR. However, in the high-income group, tumor

219   excision surgery did not affect the post-RT mortality rate.

220   Hagedoorn et al. (2016) reported that among men aged 40–64 years with HNC in Belgium,

221   survival was significantly lower for men with a low SEP and living in deprived areas. The

222   differences in survival between the low- and high-SEP groups appeared less pronounced in more

223   deprived municipalities (Hagedoorn et al., 2016). The main difference between our study and the

224 study by Hagedoorn et al. (2016) is that we included both working-age men and women with HNC

225 treated with RT. The difference in post-RT survival between low- and high-income groups was

226 higher in more deprived areas in Taiwan, such as Eastern Taiwan.

227   Men exhibited 104.9% greater HNC-associated mortality than did women. Many studies have

228 confirmed that survival is poorer among men with HNC than among women with HNC (Choi et

229 al., 2016; Chu et al., 2016; Olsen et al., 2015; Osazuwa-Peters et al., 2016), which is consistent

230 with the results of the present study. However, we discovered a much higher HR in men than that

231 reported previously, which may have resulted from the following reasons: (1) women are more

232 likely than men to seek medical care and comply with treatment regimens (Osazuwa-Peters et al.,

233 2016), and (2) men are more likely to chew betel nut, which increases the risk of oral squamous

234 cell carcinoma, an aggressive form of HNC (Tung et al., 2013; Yang & Lin, 2017). Approximately

235 10% of Taiwan's population habitually chews betel nut (~2 million people) (Ko et al., 1992). This

236 percentage is higher in Southern and Eastern Taiwan, particularly among men (men: 16.5%;

237 women: 2.9%), those of lower SES, habitual smokers, alcoholics, and aborigines (Chen et al.,

238 2017; Chi-Pang et al., 2009).

239   We noted that patients treated with either cisplatin or 5-fluorouracil chemotherapy had 50.4%

240 greater risk of mortality than did who were not treated with chemotherapy. Cisplatin and 5-

241 fluorouracil constitute standard chemotherapy for recurrent or metastatic squamous cell carcinoma

242 of head and neck (SCCHN) (Tahara et al., 2014). Because more than 90% of HNCs in Taiwan are

243 squamous cell carcinoma, we selected cisplatin and 5-fluorouracil as the chemotherapeutic

244 variables. We assumed that most HNC patients received cisplatin and 5-fluorouracil to treat

245 recurrent or metastatic SCCHN. Therefore, patients treated with chemotherapy had lower survival

246 rate.

247   Intensity-modulated RT (IMRT) and VMAT provide superior target coverage, greater

248 efficiency, fewer complications, shorter therapy duration, and less influence on the quality of life

249 than do conventional RT and three-dimensional conformal RT (Duarte et al., 2014; Lin et al., 2014;

250 Tribius & Bergelt, 2011). IMRT and VMAT have rapidly replaced conventional RT and three-

251 dimensional conformal RT since 2009 in Taiwan (Bedford & Warrington, 2009; OuYang et al.,

252 2016; Zhang et al., 2015). Therefore, the cutoff point in the present study was 2009.

253

254 **Limitations**

255 Given that RT and CT for HNC are mostly outpatient treatments in Taiwan, the presence of

256 dependents of working-age caregivers, such as children or parents, may have worsened treatment

257 compliance. Although patients from deprived areas, such as Eastern Taiwan, often travel to other

258 regions to receive medical services, the NHIRD only tracks the region of insurance application,

259 which may be a patient's location of employment, rather than region of residence. Furthermore,

260 the tumor–node–metastasis stage, nutritional status, education level, behaviors and habits, race,

261 and faith of patients are unavailable in the NHIRD. The RT protocol type (conventional RT, three-

262 dimensional conformal radiation therapy, IMRT, or VMAT), either palliative or curative, also

263 affects the survival rate of HNC patients (Marta et al., 2014). We focused on the survival of HNC

264 patients who received a complete RT course; however, the RT protocol was the NHIRD. Newer

265 RT techniques, such as IMRT and VMAT, may not be simultaneously introduced in all four

266 geographical areas of Taiwan. In a relatively deprived area such as Eastern Taiwan, the

267 introduction of such techniques may well be delayed. This uncontrolled bias might confound the

268 higher mortality discovered in Eastern Taiwan. Several studies have shown that being human

269 papillomavirus positive is associated with better survival in patients with oropharyngeal squamous

270 cell cancer (D'Souza et al., 2016; Young et al., 2015). These variables were not controlled or

271 analyzed in the present study.

272

CONCLUSION

Income and residential area significantly affected the survival rate of HNC patients receiving RT

in Taiwan. The highest income group had the best survival rate, regardless of geographical area.

The negative predictive factors for survival in HNC patients included being male, tumor with oral

origin, RT initiation before 2009, no tumor excision surgery, use of chemotherapy, and use of

mandibulectomy or maxillectomy.

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Figure 1

Definition of residential area in Taiwan

Red is designated for the northern area, green for the central, yellow for the southern, and blue for the eastern and offshore islands.

Tropic of cancer

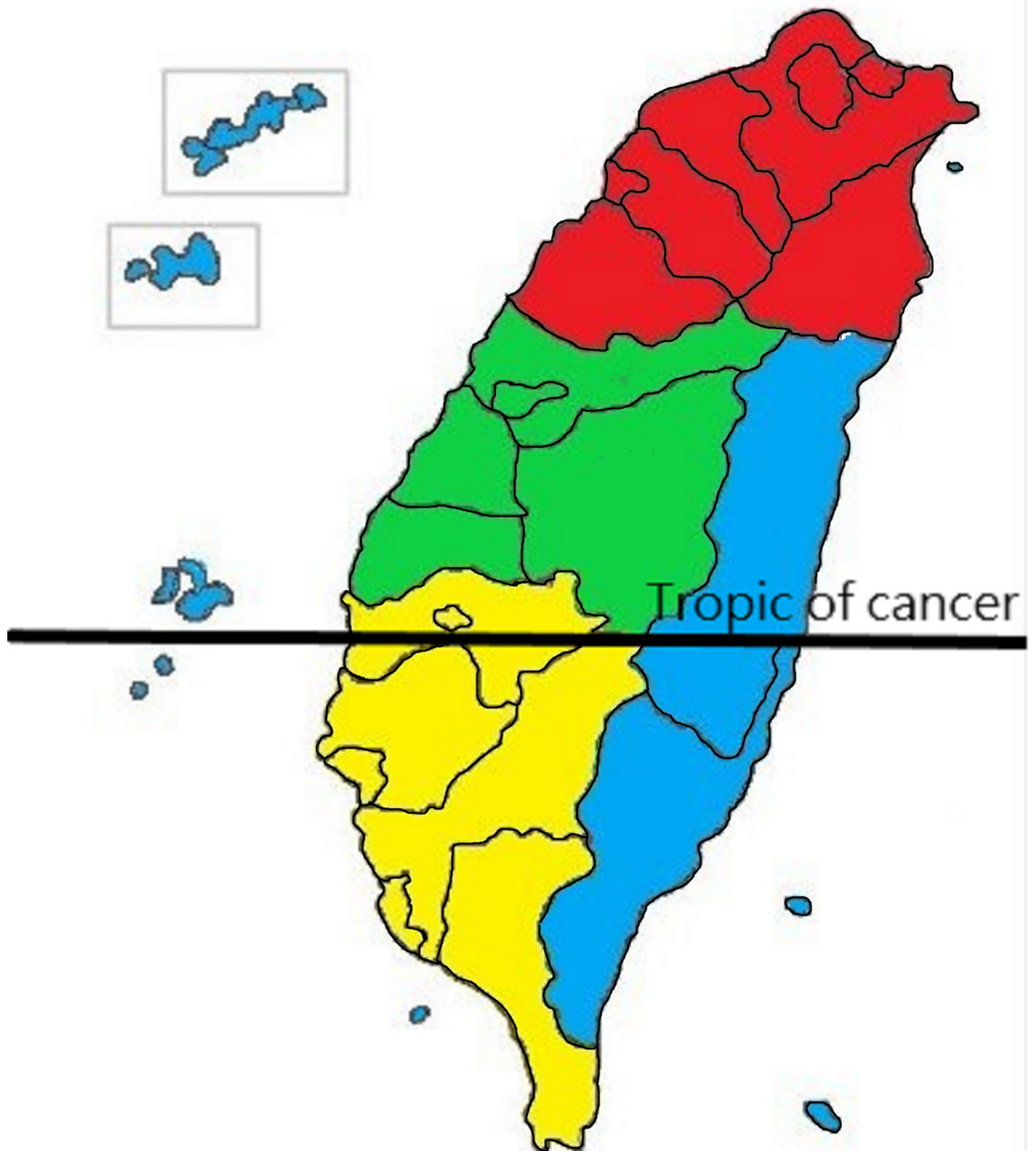



Figure 2

Description and comparisons of post-radiotherapy survival of head and neck cancer between geographic areas and income levels.

(A) Comparisons between low, medium and high income level in four geographic areas. (B)

Comparisons between northern, central, southern and eastern areas in three income levels.

Geographic region	Income		
	Low income	Medium income	High income
	Survival (%)	Survival (%)	Survival (%)
Northern	54.2%	55.9%	65.3%
Central	47.6%	50.5%	58.4%
Southern	44.2 %	47.6%	56.2%
Eastern	38.7%	40.8%	57.0%
All	48.6%	50.8%	61.2%

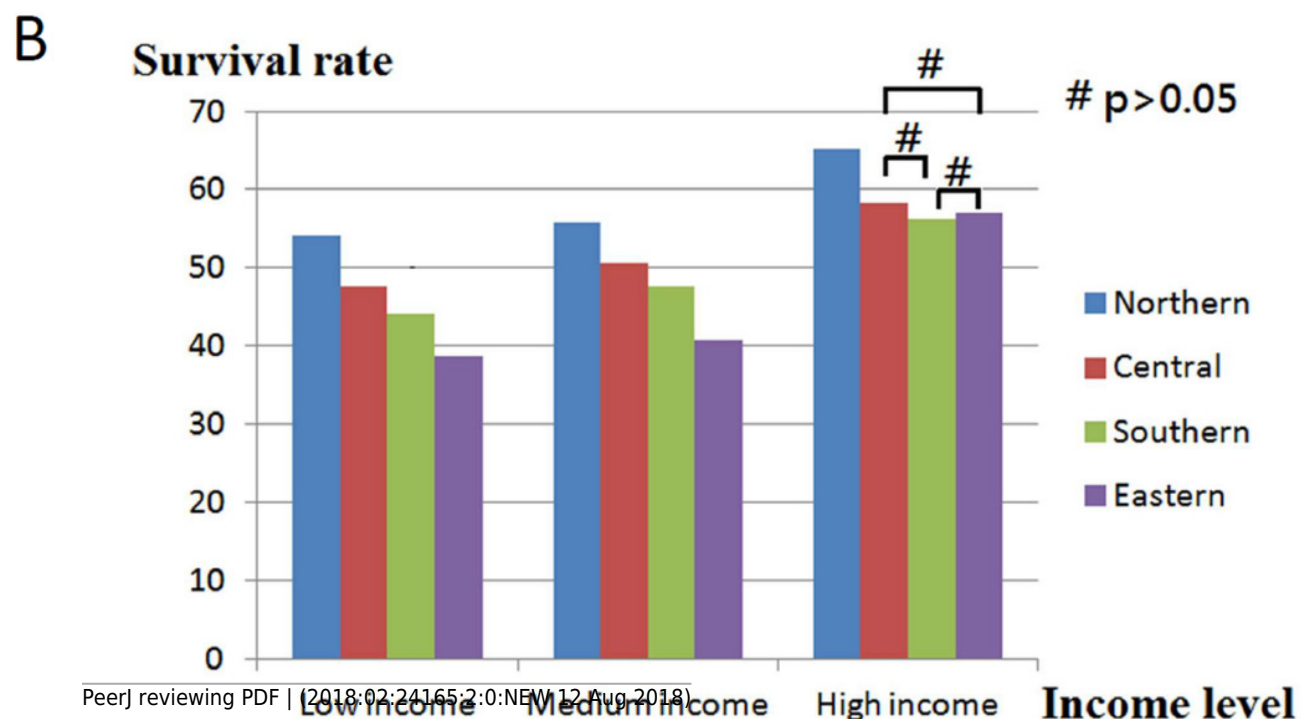
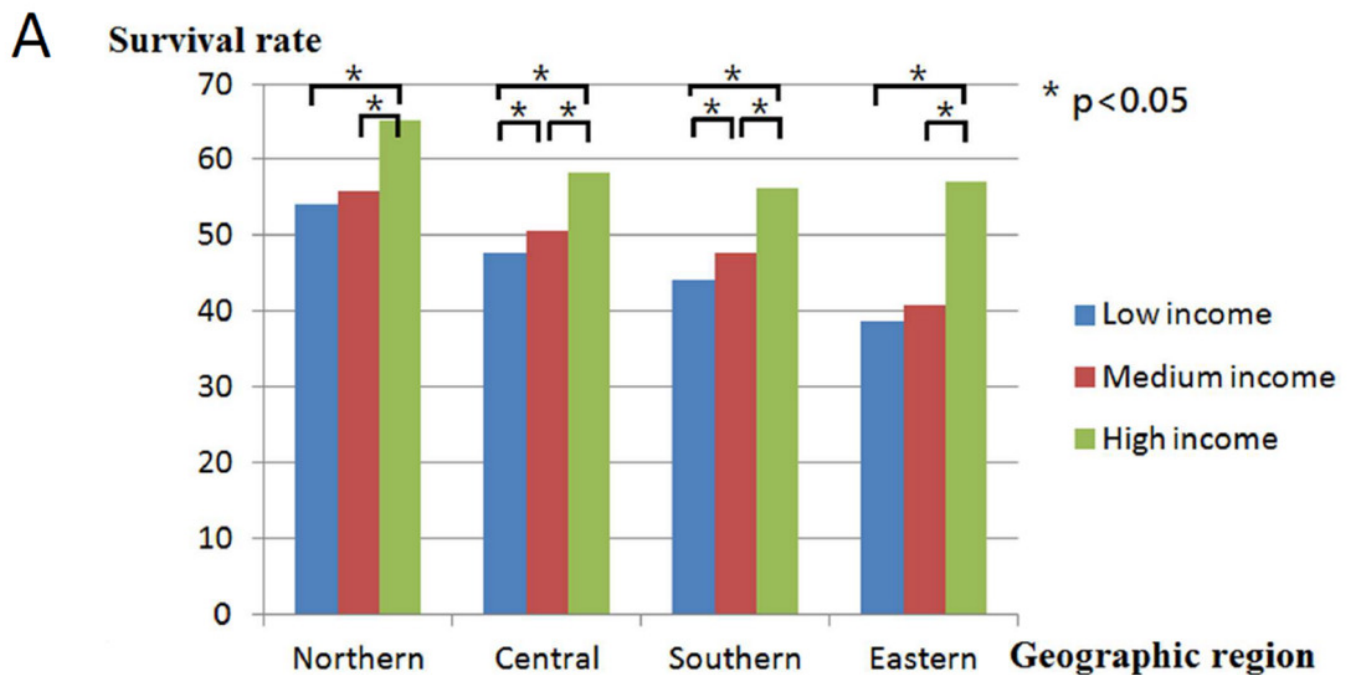



Figure 3

Kaplan–Meier survival curve of HNC patients post radiotherapy.

(A) Kaplan–Meier survival curve of HNC patients post radiotherapy (N=40985). (B) Kaplan–Meier survival curves of HNC patients post radiotherapy for different residential area. (C)Kaplan–Meier survival curves of HNC patients post radiotherapy for different income level.

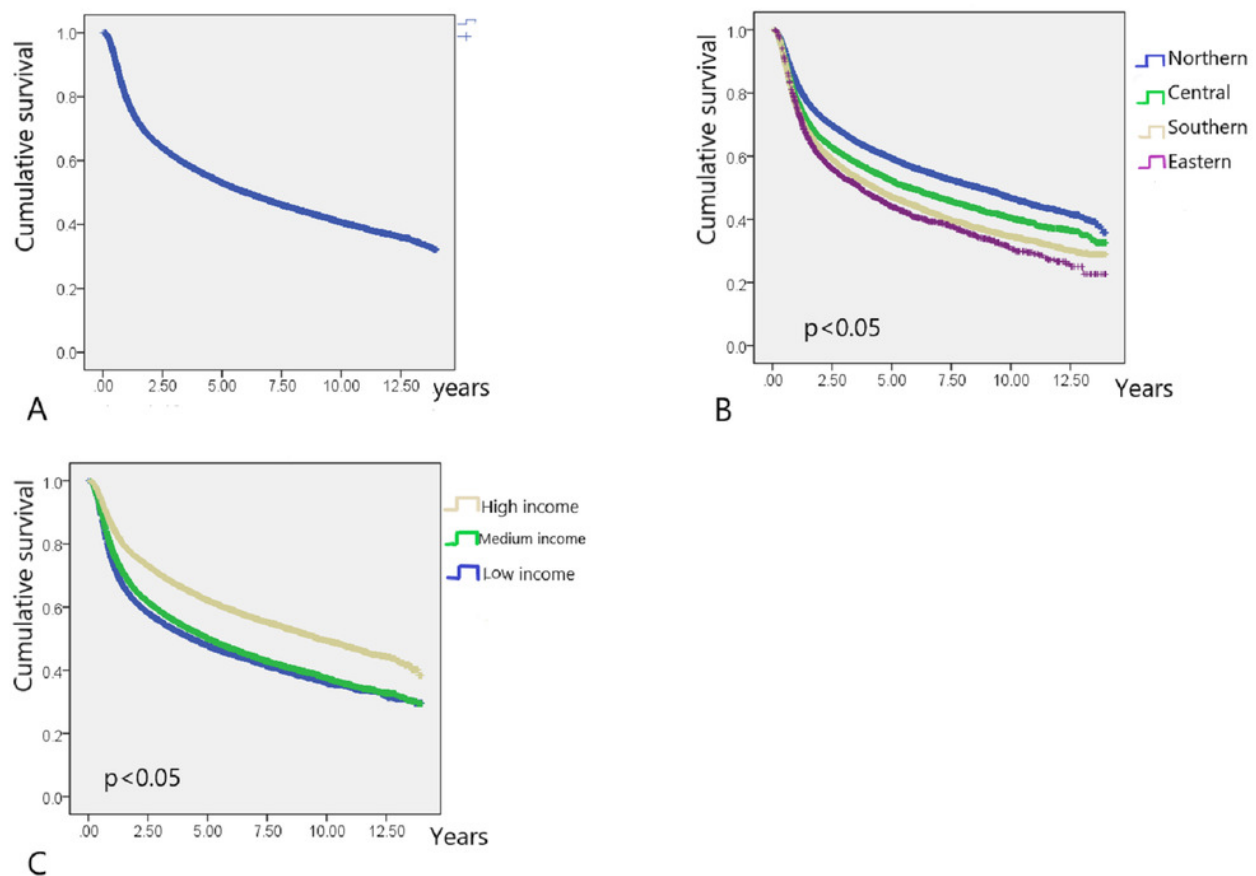
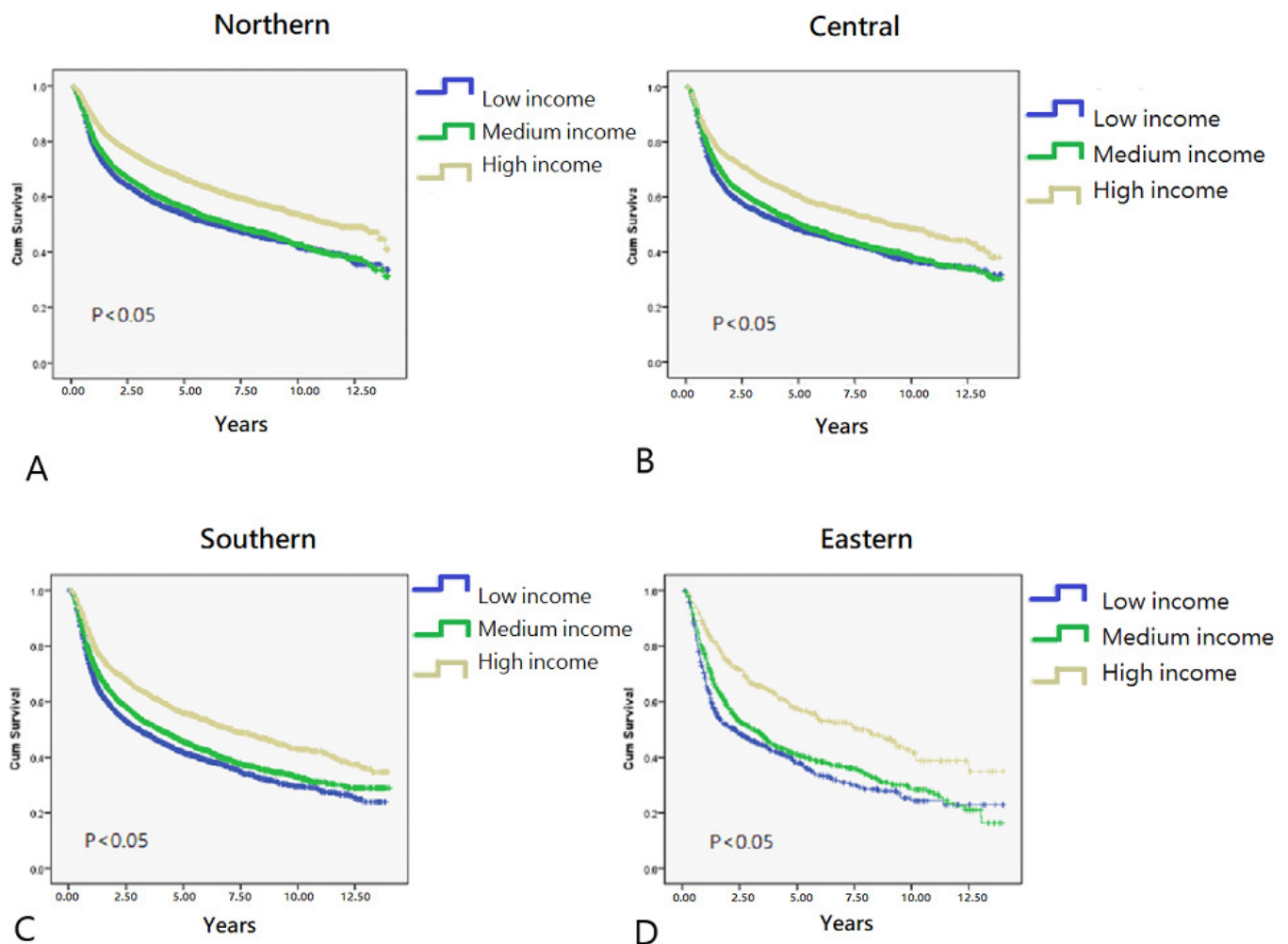



Figure 4

Kaplan–Meier survival curves in different residential area.

(A) Northern area of Taiwan. (B) Central area of Taiwan. (C) Southern area of Taiwan. (D) Eastern area of Taiwan.

Baseline characteristics

Variables	Income				p-value
	Low (*n*=12481)	Medium (*n*=16168)	High (*n*=12336)	Total (*n*=40985)	
Mean age, yrs (±SD)	48.45 (±9.01)	49.89 (±8.46)	49.17 (±8.50)	49.23 (±8.66)	<0.001
Residential area Cases (%)					
Northern	4810(38.5%)	5151(31.9%)	6093(49.4%)	16054	<0.001
Central	2952(23.7%)	4767(29.5%)	2451(19.8%)	10170	
Southern	4112(32.9%)	5443(33.6%)	3327(27.0%)	12882	
Eastern	607 (4.9%)	807(5.0%)	465(3.8%)	1879	
Sex					0.997
Male (%)	M: 87.35%	M: 87.29%	M: 87.37%	M: 87.33%	
Female (%)	F:12.65%	F: 12.71%	F:12.63%	F:12.67%	
With Tumor surgery (Around 3 months of index day)	9.1%	9.3%	7.8%	8.8%	<0.001
With mandibulectomy or maxillectomy surgery(in 3 months before index day)	5.02%	5.40%	3.74%	4.78%	<0.001
Timing of receiving R/T Before 2009 (%)	55.04%	57.42%	57.50%	56.72%	<0.001
Origin : Oral cavity (%)	44.85%	45.58%	36.74%	42.70%	<0.001
Combine chemotherapy(%)	77.2%	75.3%	76.6%	76.3%	0.01

Median survival years

Residential area	Income level	Cases	Survival (years)		
			Median	SD	95% CI
Northern		16054	8.680	.218	8.252-9.108
	Low	4810	6.360	.341	5.691-7.029
	Medium	5151	7.070	.324	6.435-7.705
	High	6093	11.610	.436	10.756-12.464
Central		10170	5.740	.199	5.351-6.129
	Low	2952	4.450	.311	3.841-5.509
	Medium	4767	5.120	.239	4.652-5.588
	High	2451	9.140	.576	8.011-10.269
Southern		12882	4.300	.123	4.060-4.540
	Low	4112	3.070	.160	2.757-3.383
	Medium	5443	3.950	.168	3.621-4.279
	High	3227	7.080	.379	6.336-7.824
Eastern		1879	3.670	.258	3.165-4.175
	Low	607	2.300	.354	1.607-2.993
	Medium	807	3.080	.297	2.498-3.662
	High	465	7.690	.906	5.914-9.466
Total case		40985	6.030	.101	5.831-6.229

Pair comparison of survival curve.

	Residential area	Income	Low		Medium		High	
			Chi-square	p value	Chi-square	p value	Chi-square	p value
Log Rank (Mantel-Cox)	Northern	Low			5.123	.024	202.379	<0.01
		Medium	5.123	.024			146.615	<0.01
		High	202.379	<0.01	146.615	<0.01		
	Central	Low			5.779	.016	84.647	<0.01
		Medium	5.779	.016			63.549	<0.01
		High	84.647	<0.01	63.549	<0.01		
	Southern	Low			20.904	<0.01	174.397	<0.01
		Medium	20.904	<0.01			95.323	<0.01
		High	174.397	<0.01	95.323	<0.01		
	Eastern	Low			4.380	.036	54.975	<0.01
		Medium	4.380	.036			36.183	<0.01
		High	54.975	<0.01	36.183	<0.01		

Multivariate Cox proportional hazards model

	Adjusted Hazard ratio	95% CI	P
Random effect of income			
High			
Medium	1.369	1.320-1.420	<0.001
Low	1.514	1.458-1.572	<0.001
Residential area			
Northern			
Central	1.128	1.087-1.171	<0.001
Southern	1.402	1.355-1.451	<0.001
Eastern	1.454	1.362-1.552	<0.001
Random effect of gender			
Female			
Male	2.049	1.943-2.162	<0.001
Random effect of tumor origin			
Origin :Non-oral			
Origin:Oral	1.660	1.609-1.712	<0.001
Random effect of tumor excision surgery			
with surgery			
without surgery	1.181	1.120-1.246	<0.001
Random effect of receiving R/T timing			
After 2009			
Before 2009	1.219	1.180-1.259	<0.001
Random effect of mandibulectomy or maxillectomy surgery			
With			
Without	1.215	1.137-1.299	<0.001
Random effect of chemotherapy			
Without chemotherapy			
With chemotherpay	1.504	1.452-1.558	<0.001