# Impact of Comorbidity on Survival for Locally Advanced Head and Neck Cancer Patients Treated by Radiotherapy or Radiotherapy plus Chemotherapy

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**Background:** The aim of this study was to investigate the impact of comorbidity on survival for patients with locally advanced head and neck squamous cell carcinoma (HNSCC).

**Methods:** A total of 214 patients with locally advanced HNSCC, treated with radiotherapy (RT) or RT plus chemotherapy (CT) from January 2000 to December 2003, were included. Comorbidity was scored by the Charlson comorbidity index (CCI). The patient-, tumor-, and treatment-related variables were recorded and overall survival (OS) and disease specific survival (DSS) were calculated.

**Results:** Seventy-one patients (33%) had at least one comorbid condition. The most common comorbid condition was liver disease (13.6%). Higher CCI scores were not significantly correlated with exposure to smoking, alcohol, or betel quid, but were associated with older age, fewer years of education years, and no CT ($p < 0.05$). The 3-year OS and DSS rates were, respectively, 21.9% and 24.4% for all patients; 25.9% and 26.9% for those with CCI scores of 0, 21.8% and 28.3% for scores of 1, and 3.5% and 7.5% for scores ≥ 2. Multivariate analysis revealed that a CCI score ≥ 2, stage IV disease, a RT dose < 70 Gy, and no CT were significant predictors of poorer OS and DSS.

**Conclusions:** Our data reveal the significant survival impact of comorbidity on patients with locally advanced HNSCC treated by RT or RT plus CT.

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**Key words: comorbidity, Charlson comorbidity index, head and neck cancer, radiotherapy, chemotherapy**

Cigarette smoking and alcohol drinking are well known risk factors in the development of squamous cell carcinoma of the head and neck (HNSCC). Besides the carcinogenesis effect, the two substances are also associated with other significant systemic comorbidities such as pulmonary, cardiovascular, hepatic, and metabolic diseases.[1,2] However, in Southeast Asia, including Taiwan, another substance, betel quid, also plays an important role in the etiology of HNSCC.[3,4]

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It has been estimated that 400-600 million people worldwide consume betel quid. The prevalence of betel quid chewing in the Taiwanese population is higher than 10%.[5] Recently, synergistic effects of betel quid chewing with cigarette smoking and alcohol drinking were found not only in the development of the upper aerodigestive cancer but also in the progression of some chronic diseases such as chronic hepatitis, liver cirrhosis and peptic ulcer.[6-8]

Data from North American and European studies have shown the important role of comorbidity in the survival and complications in HNSCC patients.[9-18] In contrast, the patterns and prevalence of comorbidity and its effect on the treatment outcome of HNSCC patients in areas with high prevalences of betel quid chewing have seldom been explored. In this study, we enrolled patients with locally advanced HNSCC treated by radiotherapy (RT) alone or RT plus chemotherapy (CT) at a single institution in southern Taiwan, and used the well validated Charlson comorbidity index (CCI) to describe their comorbidity.[19] The patterns and prevalence of comorbidity and its prognostic values on overall survival (OS) and disease specific survival (DSS) were investigated.

## METHODS

Patients eligible for the study were those with biopsy-proven stage III or IV [according to American Joint Committee on Cancer (AJCC) staging system published in 2002] HNSCC of the oral cavity, oropharynx, hypopharynx or larynx treated with primary RT or RT plus CT. Patients with recurrence or distant metastasis of the disease were excluded from the study. From January 2000 to December 2003, a total of 214 consecutive patients referred to the department of Radiation Oncology at Kaohsiung Chang Gung Memorial Hospital, a tertiary medical center in southern Taiwan, were enrolled. The hospital's review board approved the study. The patient characteristics, history of exposure to cigarettes, alcohol, and betel quid, and treatment related variables are shown in Table 1.

The median age was 51 years (range, 28 to 91 years). Most patients were male (98%), married (79%), and had stage IV disease (91%). The primary tumor sites included the oral cavity (38%), oropharynx (31%) and hypopharynx/larynx (31%). The prevalence rates of patients who smoked, drank alcohol, and chewed betel quid were 88%, 78%, and 74%, respectively. One hundred and eighty patients (84%) presented with a Karnofsky performance status (KPS) score ≥ 80. One hundred and nine patients (51%) were irradiated with the conventional 2D technique and the others by the 3D conformal technique. The median dose was 70 Gy (range: 20-80 Gy). One hundred and fourteen patients (53%) received a combination of RT with systemic CT. The prescribed regimen of CT was an infusion of cisplatin 80-100 mg/m$^2$ on day 1 and continous intravenous infusions of 5-Flurouracil 800-1000 mg/m$^2$/24 hours on days 1 through 4 each cycle. One cycle of CT was received by 27 patients (23.7%), two by 44 patients (38.6%),

**Table 1.** Patient Characteristics Based on the Charlson Comorbidity Index (CCI)

| Variables | CCI score | | | | |
|---|---|---|---|---|---|
| | Total | 0 | 1 | ≧ 2 | *p* value |
| Patient number | 214 | 143 (67%) | 39 (18%) | 32 (15%) | – |
| Median age (yr) | 51 | 46 | 61 | 59 | < 0.01 |
| Men | 210 (98%) | 141 (98%) | 39 (100%) | 30 (94%) | NS |
| Smoking, yes | 188 (88%) | 128 (89%) | 33 (85%) | 27 (84%) | NS |
| Alcohol drinking, yes | 167 (78%) | 111 (78%) | 29 (74%) | 27 (84%) | NS |
| Betel quid chewing, yes | 159 (74%) | 106 (74%) | 30 (77%) | 23 (72%) | NS |
| Married | 169 (79%) | 112 (78%) | 29 (74%) | 28 (88%) | NS |
| Education ≤ 6 years | 117 (55%) | 70 (49%) | 25 (64%) | 22 (69%) | 0.02 |
| Employed | 59 (28%) | 42 (29%) | 10 (26%) | 7 (22%) | NS |
| KPS < 80 | 34 (16%) | 20 (14%) | 7 (18%) | 7 (22%) | NS |
| AJCC stage IV | 195 (91%) | 131 (92%) | 36 (92%) | 28 (88%) | NS |
| T4 stage | 157 (73%) | 104 (73%) | 33 (84%) | 20 (63%) | NS |
| N1-3 stage | 176 (82%) | 121 (85%) | 28 (72%) | 27 (85%) | NS |
| Tumor site | | | | | |
| Oral cavity | 82 (38%) | 57 (40%) | 13 (33%) | 12 (38%) | NS |
| Oropharynx | 67 (31%) | 43 (30%) | 14 (36%) | 10 (31%) | NS |
| Hypopharynx/Larynx | 65 (31%) | 43 (30%) | 12 (31%) | 10 (31%) | NS |
| RT dose, ≥ 70 Gy | 106 (49%) | 76 (53%) | 17 (44%) | 13 (41%) | NS |
| RT technique | | | | | |
| 2D technique | 109 (51%) | 74 (52%) | 18 (46%) | 17 (53%) | NS |
| 3D technique | 105 (49%) | 69 (48%) | 21 (54%) | 15 (47%) | NS |
| Combination with CT | 114 (53%) | 90 (63%) | 16 (41%) | 8 (25%) | < 0.01 |

**Abbreviations:** KPS: Karnofsky performance status; AJCC: American Joint Committee on Cancer staging system published in 2002; RT: radiotherapy; 2D: two-dimensional; 3D: three dimensional; CT: chemotherapy.

and more than two by 43 patients (37.7%).

Patients were regularly followed up after RT until death or their latest follow-up appointment. The duration of survival was calculated from the last day of RT. Patients alive on the last day of follow-up were censored. Survival curves were estimated by the Kaplan-Meier method. The log rank test was used to estimate the statistical significance of differences between survival curves. The Cox proportional hazards regression model was used for multivariate analysis. Differences between variables with categorical data were examined using the chi-square test. A $p$ value < 0.05 from the two-sided test was regarded as statistically significant.

## RESULTS

### Distribution of comorbidity

The distribution of comorbidity for the 214 patients based on the CCI is demonstrated in Table 2. Seventy-one patients (33%) had at least one comorbid condition. Thirty-two (15%) of them had a CCI score ≧ 2. The most frequent comorbidity was liver disease (13.6%), followed by chronic pulmonary disease (6.1%), and peptic ulcer disease (6.1%). Ten of the 29 patients with liver disease had moderate or severe liver cirrhosis, and 19 had chronic hepatitis. Three patients (1.4%) had concomitant secondary primary cancers, all of which were in the esophagus.

**Table 2.** Comorbidity Distribution Based on the Charlson Comorbidity Index (n = 214)

| Charlson comorbidity index | Scores | Patient number (%) |
|---|---|---|
| Myocardial infarct | 1 | 3 (1.4%) |
| Congestive heart failure | 1 | 1 (0.5%) |
| Peripheral vascular disease | 1 | 0 (0%) |
| Cerebrovascular disease (except hemiplegia) | 1 | 1 (0.5%) |
| Dementia | 1 | 1 (0.5%) |
| Chronic pulmonary disease | 1 | 13 (6.1%) |
| Connective tissue disease | 1 | 1 (0.5%) |
| Ulcer disease | 1 | 13 (6.1%) |
| Mild liver disease | 1 | 19 (8.9%) |
| Diabetes (without complications) | 1 | 5 (2.3%) |
| Diabetes with end organ damage | 2 | 4 (1.9%) |
| Hemiplegia | 2 | 2 (0.9%) |
| Moderate or severe renal disease | 2 | 2 (0.9%) |
| 2nd primary tumor (non-metastatic) | 2 | 3 (1.4%) |
| Leukemia | 2 | 0 (0%) |
| Lymphoma, Multiple myeloma... | 2 | 0 (0%) |
| Moderate or severe liver disease | 3 | 10 (4.7%) |
| 2nd metastatic solid tumor | 6 | 0 (0%) |
| AIDS | 6 | 0 (0%) |

### Variables correlated with CCI score

Table 1 shows the association of patient characteristics, smoking, alcohol drinking, betel quid chewing, and cancer or treatment related variables related with the CCI score. The CCI score was not significantly correlated with exposure to cigarettes, alcohol, or betel quid. Age, years of education, and RT combined with CT were the only variables found to be significantly correlated with the CCI score. Patients with a CCI score = 1 and CCI score ≥ 2 were significantly older, had fewer years of education, and were more likely to have had no CT than patients with CCI scores of 0 ($p < 0.05$).

### Prognostic factors of survival

The 3-year OS and DSS rates were, respectively, 21.9% and 24.4% for all patients; 25.9% and 26.9% for those with CCI scores of 0, 21.8% and 28.3% for scores of 1, and 3.5% and 7.5% for scores ≥ 2 $p$ value < 0.001, Fig. 1). Post-hoc analysis showed there were statistically significant differences in the OS and DSS in the group comparisons of CCI score = 0 versus CCI score ≥ 2 and CCI score = 1 versus CCI score ≥ 2. Univariate analysis shown in Table 3 revealed that variables that were significant predictors of poorer OS and DSS included a KPS < 80, CCI ≥ 2, AJCC stage IV disease, treatment with the 2D technique, an RT dose < 70 Gy, and no CT. Age, gender, smoking, alcohol drinking, and betel quid chewing, marital status, years of education, employment, tumor site, T stage, and N stage were not significant predictors of OS or DSS. Multivariate analysis of these significant survival predictors are presented in Table 4, revealing that a CCI score ≥ 2, stage IV disease, an RT dose < 70 Gy, and no CT were significant predictors of poorer OS and DSS. The risk ratio of death was 2.7 (95% confidence interval [CI]: 1.7-4.2) for those with a CCI score ≥ 2 compared with those with a CCI score ≦1. Further stratification based on pre-treatment stage and CCI score showed that the 3-year OS and DSS rate were,

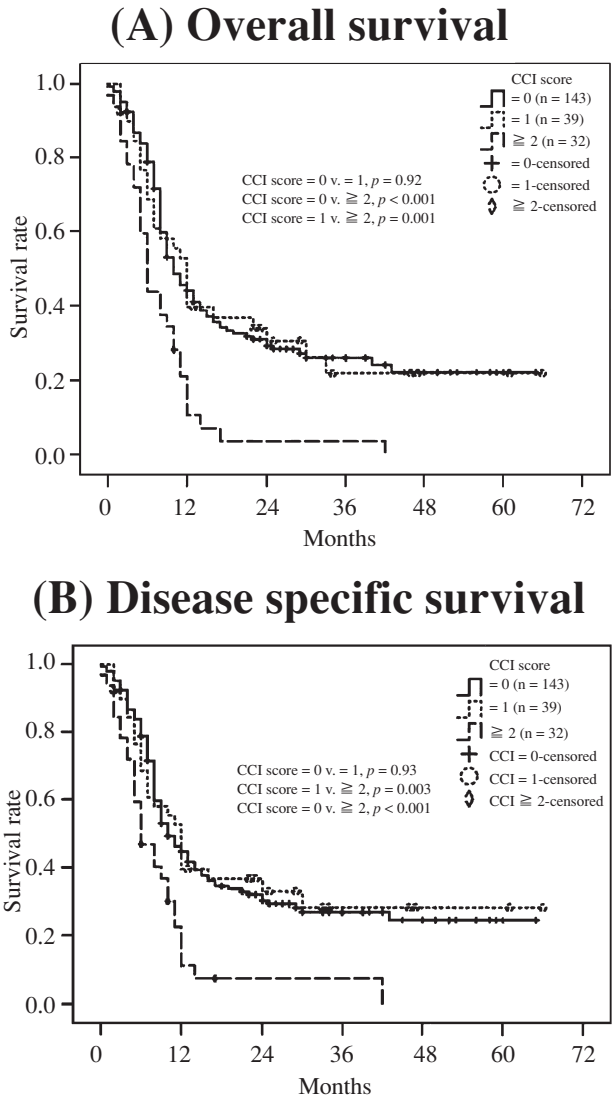


**Fig. 1** Comparisons of overall survival and disease specific survival based on the Charlson comorbidity index (CCI) score in a cohort of 214 patients with advanced head and neck cancer treated by radiotherapy or radiotherapy plus chemotherapy.

respectively 53.3% and 53.3% for those with stage III disease and a CCI score ≦ 1, 21.8% and 24.3% for stage IV and a score ≦ 1, 25.0% and 25.0% for stage III and a score ≥ 2, and 0% and 0% for stage IV and a score ≥ 2 ($p$ value < 0.001, Fig. 2), and Post-hoc analysis showed there were statistically significant differences in the OS and DSS in group comparisons of stage III and CCI score ≦ 1 versus stage IV and CCI score ≦ 1, stage III and CCI score

**Table 3.** Univariate Survival Analysis

| Variables | Overall survival | | Disease specific survival | |
|---|---|---|---|---|
| | 3 year, % | $p$ value | 3 year, % | $p$ value |
| Age | | | | |
| ≦ 40 y/o | 19.4 | 0.86 | 19.4 | 0.93 |
| 40-60 y/o | 23.7 | | 26.5 | |
| ≧ 60 y/o | 19.7 | | 22.9 | |
| Gender | | | | |
| Male | 21.8 | 0.57 | 24.3 | 0.62 |
| Female | 25.0 | | 25.0 | |
| Smoking | | | | |
| Yes | 22.7 | 0.44 | 25.6 | 0.35 |
| No | 15.4 | | 15.4 | |
| Alcohol drinking | | | | |
| Yes | 20.8 | 0.95 | 23.8 | 0.83 |
| No | 27.1 | | 27.1 | |
| Betel quid chewing | | | | |
| Yes | 22.9 | 0.83 | 26.3 | 0.96 |
| No | 17.4 | | 17.4 | |
| Marital status | | | | |
| Married | 23.5 | 0.30 | 25.7 | 0.37 |
| Unmarried | 15.9 | | 19.5 | |
| Education years | | | | |
| ≤ 6 years | 19.2 | 0.42 | 23.3 | 0.69 |
| > 6 years | 25.0 | | 25.5 | |
| Occupation status | | | | |
| Employed | 29.1 | 0.14 | 31.6 | 0.23 |
| Not employed | 18.7 | | 20.8 | |
| KPS | | | | |
| < 80 | 6.4 | 0.004 | 9.6 | 0.005 |
| ≧ 80 | 24.8 | | 27.3 | |
| CCI score | | | | |
| 0 | 25.9 | < 0.0001 | 26.9 | < 0.0001 |
| 1 | 21.8 | | 28.3 | |
| ≧ 2 | 3.5 | | 7.5 | |
| Tumor site | | | | |
| Oral cavity | 19.9 | 0.13 | 21.6 | 0.15 |
| Oropharynx | 22.9 | | 25.9 | |
| Hypopharynx/Larynx | 23.7 | | 26.3 | |
| AJCC stage | | | | |
| III | 41.4 | 0.03 | 41.4 | 0.04 |
| IV | 18.7 | | 21.5 | |
| T stage | | | | |
| T1-3 | 19.1 | 0.82 | 19.1 | 0.90 |
| T4 | 23.2 | | 26.9 | |
| N stage | | | | |
| N0 | 26.7 | 0.36 | 26.7 | 0.39 |
| N1-3 | 21.0 | | 24.0 | |
| RT technique | | | | |
| 2D technique | 18.7 | 0.04 | 19.8 | 0.03 |
| 3D technique | 25.3 | | 29.6 | |
| RT dose | | | | |
| < 70 Gy | 15.5 | 0.001 | 17.9 | 0.002 |
| ≥ 70 Gy | 29.1 | | 31.3 | |
| Combination with CT | | | | |
| No | 13.2 | < 0.0001 | 14.3 | < 0.0001 |
| Yes | 29.7 | | 33.4 | |

**Abbreviations:** KPS: Karnofsky performance status; CCI: Charlson comorbidity index; AJCC: American Joint Committee on Cancer staging system published in 2002; RT: radiotherapy; 2D: two-dimensional; 3D: three dimensional; CT: chemotherapy.

**Table 4.** Multivariate Survival Analysis

| Variables | Overall survival | | Disease specific survival | |
|---|---|---|---|---|
| | HR (95% CI) | *p*-value | HR (95% CI) | *p*-value |
| Age (continuous) | 1.0 (0.9-1.0) | 0.23 | 1.0 (0.9-1.0) | 0.17 |
| Gender (Female *v.* Male) | 2.8 (0.8-9.7) | 0.10 | 2.6 (0.7-8.9) | 0.13 |
| Smoking (No *v.* Yes) | 0.9 (0.5-1.7) | 0.78 | 0.9 (0.5-1.8) | 0.83 |
| Alcohol drinking (No *v.* Yes) | 0.8 (0.5-1.4) | 0.44 | 0.8 (0.5-1.4) | 0.44 |
| Betel quid chewing (No *v.* Yes) | 1.1 (0.7-1.7) | 0.77 | 1.0 (0.6-1.6) | 0.96 |
| Marital status (unmarried *v.* married) | 0.9 (0.6-1.3) | 0.97 | 1.0 (0.7-1.6) | 0.94 |
| Education years (≤ 6 *v.* > 6 years) | 0.9 (0.6-1.3) | 0.61 | 0.9 (0.7-1.4) | 0.80 |
| Occupation status (Not employed *v.* Employed) | 1.0 (0.7-1.5) | 0.96 | 1.0 (0.7-1.6) | 0.83 |
| KPS (≧ *v.* < 80) | 1.4 (0.9-2.3) | 0.15 | 1.5 (0.9-2.4) | 0.12 |
| CCI score (0-1 *v.* ≧ 2) | 2.7 (1.7-4.2) | < 0.001 | 2.4 (1.5-3.8) | < 0.001 |
| Tumor site (Oral cavity *v.* Non-oral cavity) | 0.7 (0.5-1.1) | 0.15 | 0.8 (0.5-1.1) | 0.17 |
| AJCC (III *v.* IV) | 2.3 (1.2-4.7) | 0.02 | 2.2 (1.1-4.4) | 0.03 |
| T stage (T1-3 *v.* T4) | 0.9 (0.6-1.4) | 0.71 | 0.9 (0.6-1.3) | 0.49 |
| N stage (N0 *v.* N1-3) | 1.4 (0.9-2.2) | 0.17 | 1.4 (0.8-2.2) | 0.20 |
| RT technique (2D *v.* 3D technique) | 0.9 (0.6-1.3) | 0.46 | 0.9 (0.6-1.2) | 0.40 |
| RT dose (≥ 70 *v.* < 70 Gy) | 1.5 (1.1-2.1) | 0.01 | 1.5 (1.1-2.1) | 0.02 |
| Combination with CT (Yes *v.* No) | 1.8 (1.3-2.6) | 0.001 | 1.9 (1.3-2.7) | 0.001 |

**Abbreviations:** HR: hazard ratio; CI: confidence interval; KPS: Karnofsky performance status; CCI: Charlson comorbidity index; AJCC: American Joint Committee on Cancer staging system published in 2002; RT: radiotherapy; 2D: two-dimensional; 3D: three dimensional; CT: chemotherapy.

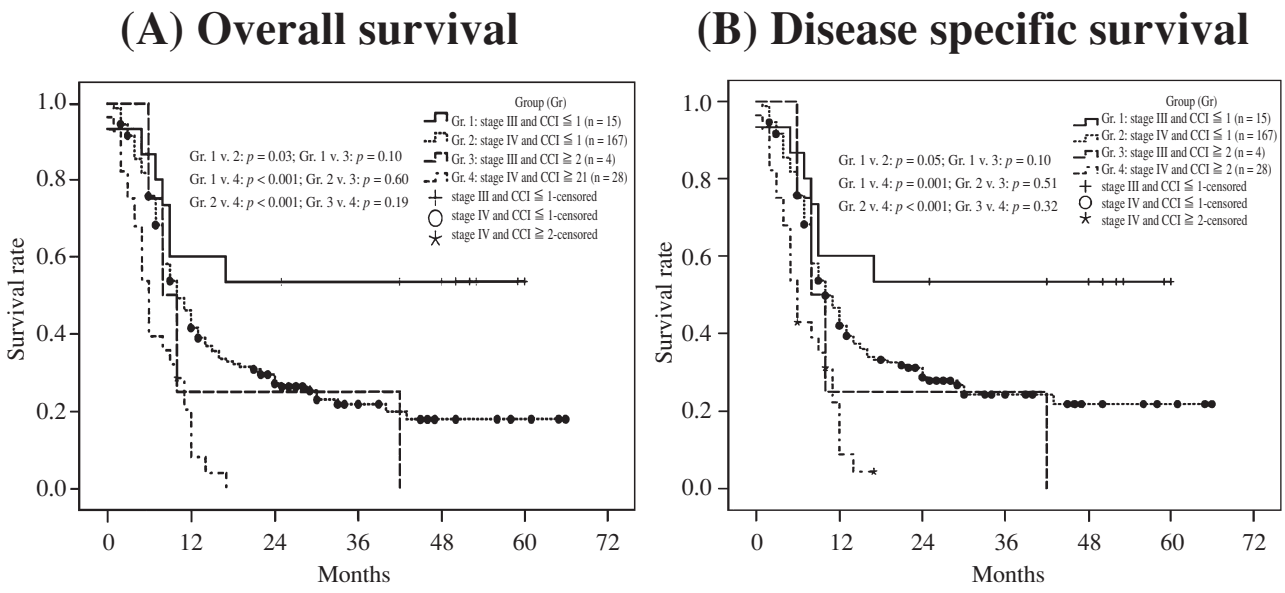


**Fig. 2** Comparisons of overall survival and disease specific survival based on the stage and Charlson comorbidity index (CCI) score in a cohort of 214 patients with advanced head and neck cancer treated by radiotherapy or radiotherapy plus chemotherapy.

≦ 1 versus stage IV and CCI score ≥ 2, and stage IV and CCI score ≦ 1 versus stage IV and CCI score ≥ 2.

## DISCUSSION

Comorbidity burden may vary among people in different geographic regions or races. Racial disparity in treatment outcomes of patients with HNSCC have been observed between American white people and African-American people.[20] Chen et al found laryngeal cancer patients of Hispanic origin had significantly less comorbidity compared with Caucasian and African-American patients.[17] Paleri et al pointed out that comorbidity should be taken into account when treatment results across regions and countries are compared in patients with HNSCC.[12]

This study describes for the first time the patterns and prevalence of comorbidity and its prognostic value on survival for HNSCC patients in an area with a high prevalence of betel quid chewing. Most studies on this subject are from Caucasians or areas where tobacco and alcohol are the potential etiologies of HNSCC and related chronic diseases. The prevalence of comorbidity in these studies ranged from 50 to 70%, which might vary according to the different comorbidity indexes used.[11-18] Rogers et al used the Adult Comorbidity Evaluation (ACE-27) and found 53% of 157 patients with HNSCC had at least one comorbidity.[18] Piccirillo et al studied the comorbidity of 7131 HNSCC patients from the Surveillance Epidemiology and End Results (SEER) database in the U.S.A. and found prevalence rates of comorbidity of 34.6%, 21.2%, 12.7%, 9.5%, and 22.1% for CCI scores of 0, 1, 2, 3, and ≧ 4, respectively.[21] We also used the CCI score to define comorbidity because of its predictive ability and relative ease of derivation but observed the prevalence and severity of comorbidity in our patients was much lower than those in previous studies. Only 33% patients had a CCI score ≧ 1, and 15% had a CCI score ≧ 2.

Cardiovascular and pulmonary diseases are the most common comorbid conditions in data on Caucasians. In current study, the most frequent comorbid condition was liver disease, followed by pulmonary and gastrointestinal disease. It was not surprising to find liver disease was the leading comorbid condition in our cohort. Epidemiological research has demonstrated Taiwan is an endemic area for viral hepatitis, especially hepatitis B virus and hepatitis C virus infections.[22,23] In addition, the combined effects of betel quid chewing, smoking, and alcohol drinking with virus infection on chronic hepatitis and liver cirrhosis have been observed in Taiwanese.[6-8] Chronic hepatotoxicity induced after long-term use of betel quid has been found in some studies.[24,25]

Little doubt exists about the causal relationship between the abuse of cigarettes and alcohol and some chronic diseases in the general population. In contrast, we did not find that abuse of these substances increased the comorbidity burden in our cohort. Similar findings in other series revealed no significant correlation between alcohol/cigarette abuse and the comorbidity burden in HNSCC patients.[14,16] Population- based epidemiological research is needed to clarify this discrepancy.

A number of reports have proven the major role of comorbidity in the treatment outcome of HNSCC patients.[9-18] Feinstein et al reported on 192 patients with laryngeal cancer and found that overall survival after 5 years was 54% in the absence of comorbidity, and 15% when comorbidity was present.[9] Hall et al analyzed 655 patients with HNSCC and found patients with comorbidity had a 23% 5-year survival and those without had 59% survival.[10] Our data, focusing on a group of patients with advanced HNSCC who were treated by RT or RT plus CT, echoed this result and showed that comorbidity is an adverse survival prognostic factor.

Some reports announced that the impact of comorbidity on survival is not similar in different cancers, but may be of greatest prognostic significance among cancers with the highest survival rates and least significant in those with the lowest survival rates.[26] Alho et al stressed the differentiated prognostic impact of comorbidity in HNSCC patients, and reported that the excess risk associated with comorbidity was confined to subjects under 65 years old, and those with tongue or laryngeal tumors or stage I-II cancer.[14] In our cohort, most patients were in advanced stages and had poor survival outcomes. However, the prognostic survival impact of comorbidity was still significant and the probability of death for patients with a CCI score ≥ 2 increased to 2.7 times that of those with a CCI score ≦ 1. Further, we observed the mean survival for patients

with stage IV and a CCI score ≥ 2 was only seven months, which might indicate that a conservative, palliative schedule of RT would be advantageous to these patients.

Many clinical trials have proved the survival benefits of CT in treating HNSCC. However, patients with more comorbidity usually have poorer general health conditions, and systemic CT is riskier for them. Whether comorbidity affects the treatment selection in cancer patients is controversial.[13,14,17] We observed both comorbidity and no CT were independent poor survival predictors but more patients with high comorbidity burden were treated by RT alone than RT plus CT. Therefore, in the clinical setting, it has become a challenging and difficult issue for patients and physicians to choose a combination of CT if patients have a high comorbidity burden.

This study was a retrospective chart-based assessment and selection bias might exist in the collection of comorbidity data. However, the results show comorbidity may vary in different areas, and highlight the significant survival impact of comorbidity for patients with advanced HNSCC treated by RT or RT plus CT. The results also justify the need for prospective data collection of comorbidity in routine clinical practice with the integration of the comorbidity index into the current TNM staging system in treatment selection and outcome prediction.

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## REFERENCES

1. Blot WJ, McLaughlin JK, Winn DM, Austin DF, Greenberg RS, Preston-Martin S, Bernstein L, Schoenberg JB, Stemhagen A, Fraumeni JF Jr. Smoking and drinking in relation to oral and pharyngeal cancer. Cancer Res 1988;48:3282-7.
2. Choi SY, Kahyo H. Effect of cigarette smoking and alcohol consumption in the aetiology of cancer of the oral cavity, pharynx and larynx. Int J Epidemiol 1991;20:878-85.
3. Ko YC, Huang YL, Lee CH, Chen MJ, Lin LM, Tsai CC. Betel quid chewing, cigarette smoking and alcohol consumption related to oral cancer in Taiwan. J Oral Pathol Med 1995;24:450-3.
4. Lee KW, Kuo WR, Tsai SM, Wu DC, Wang WM, Fang FM, Chiang FY, Ho KY, Wang LF, Tai CF, Kao EL, Chou SH, Lee CH, Chai CY, Ko YC. Different impact from betel quid, alcohol and cigarette: Risk factors for pharyngeal and laryngeal. Int J Cancer 2005;117:831-6.
5. Ko YC, Chiang TA, Chiang SJ, Hsieh SF. Prevalence of betel quid chewing habit in Taiwan and related sociodemographic factors. J Oral Pathol Med 1992;21:261-4.
6. Lin HH, Wang LY, Shaw CK, Cheng ML, Chung WK, Chiang HJ, Lin TY, Chen CJ. Combined effects of chronic hepatitis virus infections and substance-use habits on chronic liver diseases in Taiwanese aborigines. J Formos Med Assoc 2002;101:826-34.
7. Hung CR, Cheng JT. Betel quid chewing damaged gastric mucosa: protective effects of cimetidine and sodium bicarbonate. Chin J Physiol 1994;37:213-8.
8. Hsiao TJ, Liao HWC, Hsieh PS, Wong RH. Risk of betel quid chewing on the development of liver cirrhosis: A community-based case-control study. Ann Epidemiol 2007;17:479-85.
9. Feinstein AR, Schimpff CR, Andrews JF, Wells CK. Cancer of the larynx: a new staging system and a reappraisal of prognosis and treatment. J Chronic Dis 1977;30:277-305.
10. Hall SF, Groome PA, Rothwell D. The impact of comorbidity on the survival of patients with squamous cell carcinoma of the head and neck. Head Neck 2000;22:317-22.
11. Borggreven PA, Kuik DJ, Langendijk JA, Doornaert P, de Bree R, Leemans CR. Severe comorbidity negatively influences prognosis in patients with oral and oropharyngeal cancer after surgical treatment with microvascular reconstruction. Oral Oncol 2005;41:358-64.
12. Paleri V, Wight RG, Davies GR. Impact of comorbidity on the outcome of laryngeal squamous cancer. Head Neck 2003;25:1019-26.
13. Reid BC, Alberg AJ, Klassen AC, Samet JM, Rozier RG, Garcia I, Winn DM. Comorbidity and survival of elderly head and neck carcinoma patients. Cancer 2001;92:2109-16.
14. Alho OP, Hannula K, Luokkala A, Teppo H, Koivunen P, Kantola S. Differential prognostic impact of comorbidity in head and neck cancer. Head Neck 2007;29:913-8.
15. Piccirillo JF. Importance of comorbidity in head and neck cancer. Laryngoscope 2000;110:593-602.
16. Singh B, Bhaya M, Zimbler M, Stern J, Roland JT, Rosenfeld RM, Har-EI G, Lucente FE. Impact of comorbidity on outcome of young patients with head and neck squamous cell carcinoma. Head Neck 1998;20:1-7.
17. Chen AY, Matson LK, Roberts D, Goepfert H. The significance of comorbidity in advanced laryngeal cancer. Head Neck 2001;23:566-72.
18. Rogers SN, Aziz A, Lowe D, Husband DJ. Feasibility study of the retrospective use of the Adult Comorbidity Evaluation index (ACE-27) in patients with cancer of the

head and neck who had radiotherapy. Br J Oral Maxillofac Surg 2006;44:283-8.
19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
20. Gourin CG, Podolsky RH. Racial disparities in patients with head and neck squamous cell carcinoma. Laryngoscope 2006:116;1093-106.
21. Piccirillo JF, Spitznagel EL, Vermani N, Costas I, Schnitzler M. Comparison of comorbidity indices for patients with head and neck cancer. Med Care 2004;42: 482-6.
22. Liaw YF, Tai DI, Chu CM, Chen TJ. The development of cirrhosis in patients with chronic type B hepatitis: a prospective study. Hepatology 1988;8:493-6.
23. Chen DS, Sung JL. Hepatitis B virus infection and chronic liver disease in Taiwan. Acta Hepatogestroenterol (Stuttg) 1978;25:423-30.
24. Singh A, Rao AR. Modulatory influence of arecanut on the mouse hepatic xenobiotic detoxication system and skin papillomagenesis. Teratog Carcinog Mutagen 1995;15:135-46.
25. Sarma AB, Chakrabarti J, Chakrabarti A, Banerjee TS, Roy D, Mukherjee D, Mukherjee A. Evaluation of pan masala for toxic effects on liver and other organs. Food Chem Toxicol 1992;30:161-3.
26. Read WL, Tierney RM, Page NC, Costas I, Govindan R, Spitznagel EL, Piccirillo JF. Differential prognostic impact of comorbidity. J Clin Oncol 2004;22:3099-103.

# 共病因子對於局部晚期頭頸癌病患接受放射治療或合併化學治療後存活率之影響

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**背 景：** 本研究目的爲探討局部晚期頭頸部鱗狀細胞癌病患，其共病因子種類及其對於病患存活之影響。

**方 法：** 研究期間從 2000 年一月至 2003 年十二月。共收集 214 位局部晚期頭頸部鱗狀細胞癌病患納入研究。共病因子依照 Charlson 共病因子指標來計分。計算分析病患、腫瘤及治療相關變因以及其對整體存活與疾病特定存活的影響。

**結 果：** 71 位 (33%) 病患至少有一種共病因子。最常見的共病因子是肝病 (13.6%)。Charlson 共病因子指標分數的增加和抽菸、喝酒、嚼食檳榔沒有關係，而是和年紀較大、教育程度較低，以及沒有接受化學治療有統計學上的相關性 ($p$ 值小於 0.05)。全部病患三年整體存活率與疾病特定存活率分別爲 21.9% 與 24.4%；而 Charlson 共病因子零分、一分、大於等於兩分的三年整體存活率與疾病特定存活率分別爲 25.9% 與 26.9%，21.8% 與 28.3%，3.5% 與 7.5%。多變項分析指出 Charlson 共病因子大於等於兩分、腫瘤分期第四期、放射治療劑量小於七十格雷、無接受化學治療是整體存活率與疾病特定存活率不良的指標。

**結 論：** 我們研究指出共病因子在不同地域可能有所不同，並強調共病因子對於局部晚期頭頸部癌症病患接受放射治療或合併化學治療後存活之影響。

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**關鍵詞：** 共病因子，Charlson 共病因子指標，頭頸癌，放射治療，化學治療

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