The Impact of Comorbidity in Head and Neck Cancer

Jay F. Piccirillo, MD, FACS

The present TNM system of cancer classification for tumors of the oral cavity, oropharynx, and larynx is based solely on tumor morphology and does not consider important patient-based prognostic factors, such as severity of coexisting diseases, illnesses, or conditions.[1-4] These additional ailments are generally referred to as *comorbidity*. Many patients with head and neck cancer have comorbidities, partly as a result of alcohol and tobacco use.[5-6] Although not a feature of the cancer itself, comorbidity is an important attribute of the patient with cancer.[7-10] Comorbidity has direct impact on the care of patients, selection of initial treatment, and evaluation of treatment effectiveness.

The following examples demonstrate how the type and severity of the comorbid ailments may impact on treatment selection and prognosis for patients with head and neck cancer. Consider the patient with an isolated supraglottic lesion and severe pulmonary insufficiency secondary to emphysema who undergoes a total laryngectomy rather than a supraglottic laryngectomy because he is deemed too sick to tolerate the pulmonary challenges created by a supraglottic laryngectomy. As another example, consider the patient with a newly diagnosed TNM Stage IV carcinoma of the larynx who was recently hospitalized for myocardial infarction and severe congestive heart failure. Although the tumor is resectable and simple reconstruction with local tissue is possible, this patient may nevertheless receive radiation therapy as his initial therapy because he is deemed too sick to tolerate surgery. Consider the next example, two patients each age 56 and with TNM Stage I carcinomas of the larynx. One patient has severe medical comorbidity consisting of insulin-dependent diabetes and has been in renal failure for six months. The other patient only suffers from mild angina easily controlled with sublingual nitroglycerin. Both patients receive external beam radiation for their carcinoma and have a complete response. However, the first patient dies approximately 18 months after the completion of therapy while the second patient survives for another 78 months. In each of these three examples, the presence of comorbid ailments affected the selection of treatment or prognosis, or both.

The data presented here derived from ongoing research conducted by the Clinical Outcomes Research Office and the Division of Head and Neck Surgical Oncology at Washington University School of Medicine and the Oncology Data Services (ODS) Office of the Barnes-Jewish Hospital, St. Louis, Missouri. The ODS registrars participated in an NCI-funded cancer registrar comorbidity education program that was previously described in this journal.[11-12] Since 1995, the ODS registrars have collected comorbidity health information on all analytical patients at the time of tumor record abstraction using the *Adult Comorbidity Evaluation-27 (ACE-27)*, a modification of the Kaplan-Feinstein Comorbidity Index.[13]

The *Adult Comorbidity Evaluation (ACE-27)* is a new, 27-item comorbidity index for use with cancer patients. The *ACE-27* was developed through a series of modifications of the *Kaplan-Feinstein Index (KFI)*. The *ACE-27* grades specific diseases and conditions into one of three groups, Grade 1, Grade 2, or Grade 3, according to the severity of organ decompensation and prognostic impact. Once the patient's

The Impact of Comorbidity on Survival (N=757).

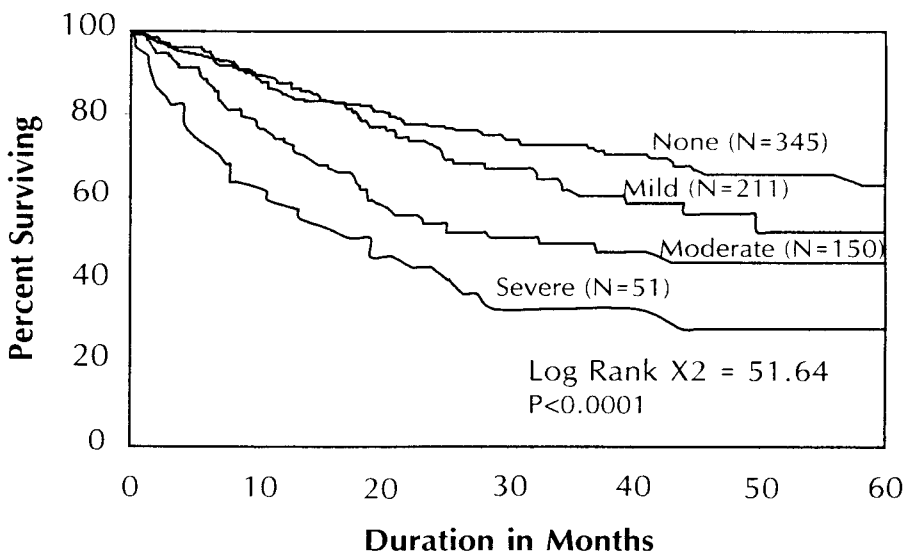

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Table 1. The Impact of Comorbidity on the Use of Radiation Therapy Only as Initial Treatment for 356 Patients with Stage III/IV Disease of Larynx, Oral Cavity and Oropharynx

Prognostic Comorbidity	Initial Treatment Therapy Radiation Only	Odds Ratio (95% CI)
Absent	84/311 (27%)	1.0
Present	23/45 (51%)	3.02 (1.61-5.69)
Total	107/356 (30%)	

Numerator = number of patients receiving radiation therapy only (N=107)
Denominator = total number of patients in each cell

individual diseases or comorbid conditions are classified, an Overall Comorbidity Score, *None, Mild, Moderate,* or *Severe,* is assigned based on the highest ranked single ailment. In the cases where two or more Grade 2 ailments occur in different organ systems or disease groupings, the Overall Comorbidity Score is designated as *Severe.* In separate research,[14] the *ACE-27* was shown to be able to define statistically significant and clinically relevant unique prognostic subgroups from a cohort of 190 newly diagnosed patients with cancer.

In the following paragraphs, the impact of comorbidity on treatment selection and prognosis for patients with head and neck cancer will be illustrated. For many patients with advanced head and neck cancer, initial treatment often involves the use of radiation therapy in combination with either surgery or chemotherapy. The American Society for Head and Neck Surgery[15] developed practice guidelines that incorporate recommendations for combined therapy for advanced lesions. However, patients with advanced lesions and severe comorbidities are often deemed "too sick" to tolerate surgery and are therefore recommended to receive radiation therapy only. The impact of comorbidity on initial treatment selection is demonstrated by comparing the rate of utilization of radiation therapy alone for patients with Stage III and IV carcinomas. Utilization rates for radiation therapy alone for patients with and without prognostic comorbidity are shown in Table 1. Of the 45 patients with prognostic comorbidity, 23 (51%) received radiation therapy as the single modality of treatment while only 84 (27%) of the 311 patients without prognostic comorbidity received radiation therapy only (X^2=10.8; p<0.001). Utilizing the odds ratio statistic, patients with TNM Stage III/IV and prognostic comorbidity are 3 times more likely to receive radiation therapy as their only initial treatment than similar patients without prognostic comorbidity. In the evaluation of the quality of cancer care, the use of single modality therapy in the setting of advanced head and neck cancer, rather than combined therapy, may erroneously be cited as poor quality of care. In fact, when the entire patient's health is considered, and not just the size of the tumor, the use of single modality therapy may actually represent sound clinical judgment. Without information on comorbidity, this important distinction in quality of care cannot be made.[16-17]

Prognostic estimates for patients with head and neck cancer are often based solely on the TNM stage of the tumor. However, as demonstrated in the figure (p. 173), survival is also based on the overall level of severity of comorbidity. The median survival for this cohort of 757 patients was 72 months. However, survival is dramatically different depending on the patient's level of comorbidity. At any point in time, patients with higher levels of comorbidity had worse survival (Log rank $X^2 = 51.64$; $p<0.001$). To examine whether this relationship between levels of comorbidity and survival remained after controlling for other important factors, a Cox proportional hazards multivariable analysis was performed.

In Table 2, the result of the Cox proportional hazards analysis is demonstrated. The prognostic impact of comorbidity was examined along with age, gender, race, TNM stage, and type of primary treatment (radiation only, surgery only, and combined radiation/surgery). After controlling for other prognostic factors, patients with moderate comorbidity had almost twice the risk (1.915), while patients with severe comorbidity had over twice the risk (2.292) of dying as patients with no comorbidity. These findings demonstrate that the impact of comorbidity on survival is not just due to other factors like age, TNM stage, or less aggressive treatment.

In conclusion, patients with head and neck cancers often have other diseases, illnesses, or conditions that can impact on treatment selection and prognosis. The failure to include an accurate description of comorbidity in hospital and population-based registries can lead to misleading conclusions about treatment effectiveness, outcomes, and quality of cancer care. The author and his colleagues at Washington University School of Medicine and Barnes-Jewish Hospital developed a comorbidity education program that successfully trains cancer registrars to code comorbidity ailments and grade overall severity accurately and efficiently from a review of the medical record. Currently, the author is developing a web-based version of this program so that registrars and other interested individuals can learn comorbidity coding through the Internet. Since registrars already seek patient demographic, tumor, and treatment information from the medical record and other health information sources, the abstraction of comorbid health information will require no additional time. The inclusion of comorbidity information in cancer registries will improve the quality of cancer statistics in this country and, ultimately, the quality of cancer care.

Note: The *ACE-27*, Coding Book, and training video, "Coding Comorbidity: The Whole Picture" are available from the author.

Table 2. Results of Cox Proportional Hazards Analysis (N= 632)

Variable	Category	Adjusted Hazards Ratio*	95% C-I	p value
Age group				
	≤ 50	1	---	---
	51-60	0.730	0.427-1.249	0.251
	61-70	1.369	0.838-2.237	0.210
	71-80	1.264	0.746-2.141	0.384
	> 80	2.491	1.325-4.683	0.005
Race				
	White	1	---	---
	Black	1.083	0.755-1.553	0.665
Comorbidity				
	None	1	---	---
	Mild	1.009	0.694-1.468	0.961
	Moderate	1.915	1.322-2.775	0.001
	Severe	2.292	1.413-3.716	0.001
TNM Stage				
	I	1	---	---
	II	1.743	1.046-2.904	0.033
	III	2.420	1.504-3.893	0.000
	IV	4.717	3.056-7.280	<0.000
Treatment				
	Combined Radiation and Surgery	1	---	---
	Surgery alone	1.061	0.722-1.561	0.762
	Radiation alone	1.695	1.082-2.653	0.021

* Adjusted hazard ratio means that the hazard ratio for each variable is adjusted for the prognostic impact of the other variables listed in the Table. Includes all 632 patients for whom necessary information was available.

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