First-Year Trends in Self-reported General Health Predict Survival in Patients With Head and Neck Cancer

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Objective: To demonstrate that first-year trends in a self-reported subjective general health assessment tool can provide prognostic information and help predict long-term survival in patients with head and neck cancer.

Design: Prospective observational cohort study.

Setting: Tertiary care center.

Patients: Four hundred three patients with head and neck cancer who were enrolled in a longitudinal outcomes project between January 1, 1995, and December 31, 2005.

Intervention: Self-reported general physical health assessments were collected using the Medical Outcomes Study 36-Item Short-Form Health Survey at diagnosis (pretreatment) and at 3, 6, 9, and 12 months after diagnosis.

Main Outcome Measures: Actuarial 5-year observed (all deaths) and disease-specific (death with cancer present) survival.

Results: Mean physical component summary (PCS) scores decreased at 3 months in all patient groups. While patients who died within the second or third year exhibited virtually no recovery, those who died within the fourth or fifth year exhibited some recovery, and those who survived 5 years or longer approached baseline PCS scores by 12 months. Shorter survival correlated with a greater net decrease in PCS score at 12 months. Groups based on pretreatment and 12-month PCS scores had significantly different survival curves. The net change in PCS score at 12 months (∆PCS) was a predictor of both observed and disease-specific survival at univariate analysis and an independent predictor of disease-specific survival in multivariate analysis.

Conclusion: First-year trends in the 36-Item Short-Form Health Survey PCS score, a self-reported subjective measure of general physical health, are predictive of long-term survival.


Although the TNM staging system is an effective predictor of cancer survival, it considers only factors directly related to the index cancer and does not consider the presence or extent of other unrelated medical conditions or the patient’s general state of health and well-being. These factors may have a meaningful effect on the management of patients with head and neck cancer from the initial assessment through treatment selection and management of complications.

Extensive work in the area of comorbidities has shown the potential usefulness of measuring the severity of comorbid illnesses as an adjunct to TNM staging, and it has been suggested that a composite TNM-comorbidity staging system may have clinical value.1 Although several studies in patients with head and neck cancer have shown that comorbidity measures correlate well with surgical complications5,9 and overall survival,4,5,7 association with disease-specific survival has been inconsistent.6,7 The usefulness of measuring comorbidities is limited because the effect of both the patient’s primary cancer and subjective sense of overall health and well-being are ignored.

Pugliano et al⁸ documented the prognostic value of symptoms in head and neck cancer. They showed that weight loss, neck lump, dysphagia, and otalgia are independent predictors of the duration of survival and created a composite symptom-severity staging system, recently referred to as the Cancer Associated Symptom Index, based on these 4 symptoms. The symptom-severity stage was noted to be independently predictive of the duration

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of survival, along with age, alcohol use, TNM stage, and comorbidity. Although measurement of cancer-related symptoms augments measures of comorbidity by better assessing the effect of the primary cancer on the patient, it fails to assess the patient’s self-perception of general health.

The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) quantifies patients’ perceptions of their general physical and mental health and, thus, reflects the relative personal burden of their combined illnesses including the index cancer. The SF-36, a self-report survey completed by the patient, assesses multiple concepts including limitations in role, social, and physical activities as a result of pain, energy level, sense of well-being, psychological distress, health or emotional problems, and general perception of health. Subscores in each of these areas are pooled into 2 composite summary scores for statistical analysis; these scales, ranging from 0 to 100, indicate overall mental and physical health and are termed the mental component summary and the physical component summary (PCS). Unlike measurements of comorbidity, these ratings are influenced by the patient’s outlook, attitudes, environment, and social support; they may also reflect patient demographic data, such as age and annual income, that likely influence the patients’ ability to manage their cancer and other illnesses.

Our group has recently reported that in a large cohort of patients with head and neck squamous cell carcinoma (SCC) who completed the SF-36 before treatment, the PCS score was independently predictive of both observed and disease-specific survival. Unlike comorbidity assessment, which rarely changes substantially during the course of treatment, results of the SF-36 change with time as patients progress through treatment and their self-perception of their general health is altered. The primary goal of the present study was to assess whether trends in the PCS score during the first year after diagnosis can provide prognostic information and help predict long-term survival in patients with head and neck cancer.

## METHODS

This prospective observational cohort study included patients enrolled in the Outcomes Assessment Project (OAP) between January 1, 1995, and December 31, 2005. The OAP is a longitudinal study of individuals with upper aerodigestive tract cancers being managed at the Department of Otolaryngology–Head and Neck Surgery at the University of Iowa Hospitals and Clinics. The study collects patient-, disease-, and treatment-related data and, in addition, asks participants to submit a battery of health-related quality-of-life surveys as part of their outpatient clinic visits. The targeted periods for data collection during the first year are before treatment, at diagnosis, and at 3, 6, 9, and 12 months after diagnosis. During the time frame specified, 1065 of 1581 patients (67.4%) who met OAP criteria were enrolled, whereas 278 patients refused to participate and 238 were missed. The primary site was categorized as oral cavity, oropharynx, hypopharynx, larynx, or other. Pathologic stage was recorded when available; otherwise, clinical stage was used. Survival information (ie, date of last contact, and patient and disease status at last contact) is updated periodically. This study was conducted with the approval of the University of Iowa Institutional Research Review Board.

The SF-36 was used to measure patients’ perceived general health status and was included in the battery of surveys administered to participants in the OAP. This well-validated instrument assesses 8 areas of general health from which the PCS is calculated. The PCS is normalized on a scale of 0 to 100, with higher scores representing better functioning. The SF-36 provides age-matched normative data from the general population and a published effect size, with differences of 5 points or more considered clinically significant. As a part of the OAP, the SF-36 is administered at diagnosis and at 3, 6, 9, and 12 months after diagnosis. The pretreatment SF-36 results were compared with those obtained from the general population aged 55 to 64 years; these well-established normative data best represent the study cohort. Study patients were assigned to either a “lower” or “upper” group if their PCS score was below or equivalent to or was above the median PCS score for this group, respectively. These 2 categories were further divided into patients whose 12-month scores increased, decreased, or were unchanged relative to their pretreatment scores on the basis of a change of 5 points or more.

The Adult Comorbidity Evaluation–27 was used to generate an overall score categorizing comorbidity as none (0), mild (1), moderate (2), or severe (3). For this study, a reviewer retrospectively assigned OAP participants a pretreatment comorbidity score based on medical chart information that was available at or before the initiation of their cancer-directed treatment. The index condition (the head and neck cancer) was not classified as a comorbid condition.

Statistical analyses were performed using commercially available statistical software (SPSS version 14.0 for Windows; SPSS Inc, Chicago, Illinois). The change in mean PCS score from pretreatment to 12 months in each group was evaluated using the t test. The difference between groups in mean PCS scores at 12 months was assessed using analysis of variance. The actuarial method was used to calculate 5-year observed survival (the end point was death from any cause) and disease-specific survival (the end point was death with cancer present). Survival rates were calculated as a function of the patient groups reflecting their pretreatment PCS scores and how those scores changed during the first year. The Wilcoxon (Gehan) statistic was used to determine significant pairwise differences. Cox proportional hazards regression analyses were performed to determine whether the net change in PCS score at 12 months (ΔPCS) was predictive of observed or disease-specific survival or both. Results were considered statistically significant at P < .05.

## RESULTS

A pretreatment SF-36 was completed by 732 of 1065 enrolled patients; 112 of these 732 patients died during the first year, and 461 of the remaining 620 patients subsequently completed a 12-month SF-36. Of the 461 patients who provided both the pretreatment and 12-month SF-36, a PCS score could not be calculated for 58 because 1 item or more on at least 1 of the 2 surveys was missing. The remaining 403 patients were predominantly men (64.0%) and had a mean age of 58.7 years. Additional patient, tumor, and treatment characteristics are given in Table 1.

**Figure 1** shows the mean PCS scores across the first year for 351 patients grouped by primary site; patients classified as other were excluded. A similar pattern is seen for patients with cancer of the oral cavity, oropharynx, and larynx, with a large decrease in the mean PCS score at 3 months followed by recovery toward the pretreat-
ment score; the net change in mean PCS at 12 months was $-3.4$, $-3.2$, and $-2.2$, respectively, for these groups. The group with hypopharyngeal primary lesions had a lower initial PCS score, and, while the mean PCS score in this group decreased at 3 months, similarly to other groups, it ultimately increased to slightly higher than the pretreatment score, with a net change at 12 months of $0.8$.

Mean first-year PCS scores for 385 patients grouped by stage are shown in Figure 2. Patients with stage IV disease tended to have slightly lower pretreatment scores. Scores in all groups declined at 3 months, but the change was minimal in patients with stage 0 (in situ) or stage I lesions. At 12 months, patients with advanced-stage lesions (stages III and IV) had lower mean PCS scores compared with patients with early lesions (stages 0/I and II). The net change in mean PCS scores at 12 months was $-1.4$, $-2.6$, $-1.6$, and $-4.6$ for stages 0/I, II, III, and IV, respectively.

Figure 3 shows the mean PCS scores across the first year for 401 patients grouped according to treatment method.
method. Although the pretreatment and 12-month scores were similar in all 3 groups, the group who underwent only surgery exhibited a smaller decline in PCS score at 3 months and a return to baseline within 9 months, whereas the groups who received radiotherapy or chemotherapy or surgery plus radiotherapy, chemotherapy, or chemoradiotherapy exhibited a more dramatic decline at 3 months and more gradual return toward baseline.

The 375 patients who had complete comorbidity assessments were grouped according to degree of comorbidity; the mean PCS scores for these groups during the first year are shown in Figure 4. Pretreatment PCS scores decreased as comorbidity increased. The degree of decline in mean PCS score at 3 months decreased as comorbidity increased. At 12 months, the net change in mean PCS score for comorbidity was as follows: none, −4.7; mild, −2.7; moderate, −3.4; and severe, −1.6.

Figure 5 shows the mean PCS scores across the first year for 292 patients grouped by survival; living patients with less than 5 years of follow-up were excluded. The mean PCS score for each survival group decreased at 3 months, but patients who died within the second or third year exhibited virtually no recovery, whereas those who died within the fourth or fifth year exhibited some recovery, and those who survived 5 years or longer approached pretreatment status by 12 months. As survival increased across these 3 groups, the mean decline in the mean 12-month PCS score decreased; the net change in mean PCS score at 12 months was −5.8 for patients who died in the second or third year, −3.8 for patients who died in the fourth or fifth year, and −2.2, for patients who survived longer than 5 years. For informational purposes, Figure 5 additionally includes the mean PCS scores for 104 patients who were excluded from the study because they died in the first year. The mean PCS score for this group decreased sharply at 3 months and continued to decrease at 6 months. No 9- or 12-month data were available for these patients.

Patients in the study group were divided into upper and lower groups, as described in the “Methods” section. These groups were further subdivided on the basis of an increase or decrease in PCS score at the 12-month assessment. Table 2 gives the distribution of patients and mean change in PCS score in each group. Figure 6 shows the observed and disease-specific survival rates for these subgroups. Because these assessments include only patients who were alive at 12 months after diagnosis and completed an SF-36, the first-year survival rates are 100%, and subsequent 2- through 5-year survival data are higher than in groups in which patients who survived less than 1 year are included. The upper/unchanged group had the highest observed and disease-specific 5-year survival rates: 96.0% and 97.9%, respectively. The lower/down group had the lowest observed and disease-specific survival rates: 57.2% and 64.4%, respectively. The upper/down, lower/up, and lower/unchanged groups had similar survival curves; for both observed and disease-specific survival, there were no significant differences among these 3 groups. However, all other group comparisons were significantly different for both observed and disease-specific survival.
Our previous study comparing pretreatment SF-36 scores with the comorbidity index demonstrated that in a group of patients with head and neck SCC, although comorbidity was only predictive of observed survival, the SF-36 PCS score was predictive of both overall and disease-specific survival. This finding suggests that the SF-36, a self-reported measure of general health, captures prognostic information related to cancer state. Unlike comorbidity measures, the results of the SF-36 fluctuate over time as the patient’s perception of their overall well-being changes. It seems intuitive that a patient’s perception of well-being would fluctuate (e.g., during intensive cancer therapy vs after recovery from successful treatment), and it seems possible that this fluctuation may be predictive of long-term outcome. This study demonstrates that the change in self-reported health status during the first year is predictive of long-term outcome (i.e., 5-year survival).

When trends in SF-36 scores across the first year were assessed, PCS scores in 150 patients (37.2%) returned to within 4 points of their baseline, whereas scores in 166 patients (41.2%) exhibited a net decrease of at least 5 points and scores in only 87 patients (21.6%) exhibited a net increase of at least 5 points. The average net change in PCS (mean ΔPCS) was −3.1 in all patients. The most consistent general finding in all groups studied was a sharp decrease in PCS score at 3 months and a subsequent gradual increase. Because the PCS is an assessment of physical performance and adequacy, it is not surprising that this is reported by patients as being lowest just after cancer therapy vs after recovery from successful treatment. Other studies have demonstrated a similar phenomenon. Rogers et al collected SF-36 results in 48 patients undergoing surgical therapy for oral cavity SCC. At 3 months after surgery, SF-36 subscores were decreased, in particular for vitality, physical function, general health perception, and role limitation due to physical functioning. Those authors noted that the scores for vitality, general health perception, and role limitation due to physical functioning showed steady improvement at 6 and 12 months but that the score for physical functioning was unchanged at 6 months and showed limited improvement at 12 months.

In a prospective study of 67 Chinese patients undergoing primary radiotherapy to treat early-stage nasopharyngeal carcinoma (mean [SD], −3.1 [11.2]). For multivariate analyses, the 2 primary (pretreatment) factors used for staging and prognostication, that is, site and stage, were included. Treatment method was omitted from the multivariate analysis because of its close association with cancer stage. A post hoc correlational analysis showed that stage and treatment variables were correlated at the P < .001 level, with a correlation coefficient of 0.48. Univariate regression analysis demonstrated that ΔPCS between pretreatment and 12 months was a significant predictor of both observed and disease-specific survival at 5 years (P = .03 and P = .002, respectively) (Table 3). The risk ratios were 0.98 and 0.97, indicating that a 1-point increase in ΔPCS (e.g., from −10 to −9 or from +2 to +3), relative mortality risk decreased by 0.02 and 0.03 for observed and disease-specific survival, respectively. When combined with site and stage in multivariate analysis, ΔPCS continued to be a significant independent predictor of disease-specific survival (P = .003) but was no longer a significant predictor of observed survival (P = .07). For disease-specific survival, the risk ratio was 0.97; thus, the relative mortality risk decreased by 0.03 per 1-point increase in ΔPCS. Cancer stage was an independent predictor of both overall (P = .002) and disease-specific (P = .01) survival.

**Table 3. Univariate and Multivariate Analyses of Association Between Change in PCS Scores and 5-Year Survival**

<table>
<thead>
<tr>
<th>Analysis Type</th>
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<th>Disease-Specific Survival</th>
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<td>Value</td>
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<td>Multivariate (n = 385)</td>
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Abbreviation: ΔPCS, individual change in PCS; PCS, physical component summary score of the 36-item Short-Form Health Survey; RR, risk ratio.

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ryngal carcinoma, Lee et al\textsuperscript{15} asked patients to complete the SF-36 before treatment and at 2, 6, and 12 months after treatment. At 2 months after treatment, vitality, bodily pain, role limitation due to physical functioning, and role limitation due to emotional functioning subscores were significantly decreased compared with pretreatment scores. By 12 months after treatment, none of these scores was significantly different from baseline.\textsuperscript{15}

With the exception of the group with hypopharyngeal cancer (23 patients [5.7%]), site of the primary tumor had little effect on the PCS scores in our patients (Figure 1). Initially, patients with hypopharyngeal tumors had worse PCS scores; however, their scores at 12 months showed, on average, a slight increase (0.8), which was unique to the other primary tumors (and most other groups studied). It is possible that the exceptionally poor prognosis for these tumors was conveyed to patients in the pretreatment phase, lowering their self-perception and resulting in a lower pretreatment PCS score. If this is true, these patients were likely to also have lowered expectations about their outcome; surviving beyond 1 year may have exceeded their expectations, resulting in a sense of being fortunate and an overall improved sense of well-being. It is possible that these data are the result of bias owing to removal of all patients who survived less than 1 year. However, if this were the case, the pretreatment score would be expected to be similar to that for other primary tumor sites.

Compared with patients with earlier stage I to III disease, patients with stage IV disease were noted to have slightly lower pretreatment PCS scores. Patients with in situ or stage I cancer demonstrated a small decrease in mean PCS score at 3 months. Patients with stage III and IV disease ultimately had lower mean PCS scores at 12 months compared with patients with earlier stage I and III disease (Figure 2). These findings are consistent with those of Rogers et al\textsuperscript{14} who noted larger decreases in SF-36 subscores in patients with advanced- vs early-stage oral cavity SCC. They also noted a similar phenomenon in patients who underwent radiotherapy in addition to surgical therapy.\textsuperscript{14} Patients in our study treated with surgery only had a smaller decline in mean PCS score at 3 months compared with patients who underwent other types of therapy. Ultimately, the mean PCS scores for all treatment groups were the same at 12 months. This is likely because, although recovery times from surgery and radiotherapy are similar, surgical therapy was often completed within 1 to 2 weeks of the pretreatment study, whereas radiotherapy generally was administered over 7 to 8 weeks. If this were simply a timing phenomenon, however, one would expect the patients who underwent surgery and radiotherapy, with treatment often extending for 3 months or longer, to exhibit persistently lower PCS scores.

As in our previous study,\textsuperscript{11} pretreatment PCS scores correlated well with comorbidity rating using the Adult Comorbidity Evaluation–27. The net decrease in PCS score at 12 months was smallest in patients with the most severe comorbidity ratings. This may be a result of these patients having a lower expectation of their outcome because of their poorer pretreatment health. Alternatively, it may be owing to elimination of patients who survived less than 1 year. However, the distribution of patients by comorbidity rating in the present study, which excluded patients who died in the first year, is nearly identical to that in the previous study in which all patients were included regardless of survival. Thus, it would not be anticipated that absence of patients surviving less than 1 year had a consequential effect on the PCS score trends in this cohort.

When trends in PCS were assessed on the basis of survival groups (Figure 5), it was noted that shorter survival correlated with a larger decrease in mean PCS score from pretreatment to 12 months. On the basis of this finding, patients were grouped according to trends in PCS score to quantify survival. Patients’ pretreatment PCS scores were categorized as being below (lower; 293 patients [72.7%]) or equivalent to or above (upper; 110 patients [27.3%]) the median PCS score for a similarly aged (55-64 years) sample from the general population. Overall, this represents a more negative self-perception of general health than in the general population and is consistent with findings of previous studies in patients with head and neck cancer.\textsuperscript{11,14,16}

The upper and lower groups were further subdivided on the basis of an increase or decrease in PCS score at 12 months. Patients in the upper/unchanged group had the best 5-year observed and disease-specific survival rates, whereas patients in the lower/down group had the worst survival rates. Patients in the upper/down group had survival rates similar to those in the lower/up and lower/unchanged groups, which suggests that change in PCS score from pretreatment to 12 months in a single patient (ΔPCS) may be a more important predictor of survival than that patient’s pretreatment score. Univariate analysis with ΔPCS as a continuous variable revealed it to be significantly associated with both observed and disease-specific 5-year survival. Multivariate analysis demonstrated ΔPCS to be a significant independent predictor of disease-specific 5-year survival; ΔPCS trended toward but did not achieve significance as an independent predictor of observed survival (Table 3), probably because of changes in PCS scores. This likely reflects that changes in PCS scores during this time frame are primarily related to progress of and treatment of the patient’s head and neck cancer. It is important that only 38 patients (9.4%) had documented recurrence of their cancer within the first year; this group of patients with early recurring cancer alone cannot account for the observed correlation between change in PCS score and disease-specific survival.

A standard caveat for all prospective outcomes studies is selection bias toward patients who want to participate and feel healthy enough to participate. These patients are more likely to complete questionnaires adequately than are patients who refuse to participate or who drop out of the study; however, they are also more likely to be generally healthier and perhaps even more likely to have a positive outcome. The numbers given herein are based on intent to enroll; no data can be collected or presented for patients who refused participation. However, we would predict that patients who enrolled in the OAP were likely to have had somewhat better
outcomes than patients who refused to participate or who withdrew. When considering only those patients who enrolled in the OAP and survived beyond the first year, no statistically significant differences in tumor, treatment, or demographic variables were noted between the 159 patients who did not complete a 12-month SF-36 and the 403 patients included in the present analysis.

The present study demonstrates that the change in self-assessed general health during the first year after diagnosis of head and neck cancer independently predicts disease-specific 5-year survival. This may be a tool to provide additional prognostic information to patients and their clinicians. Fuller et al recently discussed conditional survival in patients with head and neck SCC. This is a method whereby survival is dynamically updated at time points along the survival curve rather than statically fixed at the time of diagnosis. For all head and neck cancer sites studied, they showed an increase in survival from 47.8% at the time of diagnosis to 64.4% in patients alive at 3 years. The present study mimics and augments the concept of conditional survival; all of the patients included were alive at 1 year and exhibited increased survival rates relative to time of diagnosis. However, their APCS over the first year further stratifies their subsequent survival and, thus, can be used to better predict long-term outcome. It may be possible to observe SF-36 results over a longer period to continually refine a patient’s prognosis, which could ultimately enable more appropriate and efficient surveillance.

This study also indicates the importance of the sense of general health and well-being in patients with head and neck cancer. The SF-36 may help to identify patients with needs beyond appropriate cancer therapy. While the PCS scores for all patients can be expected to decline at 3 months, patients who fail to demonstrate appropriate increases at 6 and 9 months may benefit from an evaluation for additional supportive resources such as speech therapy, physical therapy, and occupational therapy.

In light of the present findings, a measure of general health and well-being, such as the SF-36, used periodically may be a useful adjunct to routine care in patients with head and neck cancer, especially in the first year. It has the benefits of refining prognosis and identifying patient needs that may not be clinically obvious in a brief encounter but may have substantial effect on quality of life. The SF-36 is generally easy for patients to complete in a short time and does not require medical expertise to administer or evaluate. Further study is warranted to determine how to best integrate data from patient-reported health assessment into patient care.

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Author Contributions: Dr Funk had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Jameson, Karnell, Christiansen, and Funk. Acquisition of data: Karnell and Funk. Analysis and interpretation of data: Jameson, Karnell, Christiansen, and Funk. Drafting of the manuscript: Jameson and Karnell. Critical revision of the manuscript for important intellectual content: Jameson, Karnell, Christiansen, and Funk. Statistical analysis: Karnell and Christiansen. Obtained funding: Funk. Administrative, technical, and material support: Jameson, Karnell, and Funk. Study supervision: Funk.

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