ORIGINAL ARTICLE

Long-term Quality of Life After Treatment of Laryngeal Cancer

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Objective: To assess long-term quality of life in surviving patients with advanced laryngeal cancer.

Design: A follow-up long-term quality-of-life survey of patients randomized to the Veterans Affairs Laryngeal Cancer Study No. 268 on induction chemotherapy and radiation (CT + RT) vs surgery and RT.

Setting and Patients: Forty-six (71%) of the 65 surviving patients with prior stage III or IV laryngeal cancer who could be contacted completed the survey: 25 from the surgery and RT group and 21 from the CT + RT group. Baseline demographic and clinical characteristics among survey respondents were similar, except that those in the CT + RT group were significantly older (mean, 61.2 years) than those in the surgery and RT group (mean, 55.7 years; $P<.05$).

Interventions and Main Outcome Measures: Patients completed the University of Michigan Head and Neck Quality of Life (HNQOL) instrument, the Medical Outcomes Studies Short-Form 36 (SF-36) general health survey, the Beck Depression Inventory as well as smoking and alcohol consumption surveys.

Results: Patients randomized to the CT + RT group had significantly better ($P<.05$) quality-of-life scores on the SF-36 mental health domain (76.0) than the surgery and RT group (63.0), and also had better HNQOL pain scores (81.3 vs 64.3). Compared with patients who underwent laryngectomy, patients with intact larynges (CT + RT with larynx) had significantly less bodily pain (88.5 vs 56.5), better scores on the SF-36 mental health (79.8 vs 64.7), and better HNQOL emotion (89.7 vs 79.4) scores. More patients in the surgery and RT group (28%) were depressed than in the CT + RT group (15%).

Conclusion: Better quality-of-life scores in the CT + RT groups appear to be related to more freedom from pain, better emotional well-being, and lower levels of depression than to preservation of speech function.

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THE RESULTS of the Department of Veterans Affairs (VA) Laryngeal Cancer Study on induction chemotherapy (CT) and radiation therapy (RT) compared with surgery and RT in patients with advanced laryngeal cancer demonstrated that organ preservation can be accomplished in approximately 2 of 3 patients with advanced laryngeal cancer without significantly compromising overall survival.[1] Although it would seem that patients with laryngeal preservation would have improved quality of life, the toxic effects from chemoradiation as well as the posttreatment laryngeal scarring and edema can lead to hoarseness, dysphagia, aspiration, radionecrosis of the larynx, or pain that may affect quality of life. Several studies have demonstrated that combined RT and CT protocols are associated with significant impact on overall health-related quality of life as well as specific aspects of health related to the head and neck such as speech, swallowing,[2] pain,[3] and emotional well-being.[4] Multidimensional quality-of-life studies of head and neck cancer organ-preservation therapies, and specifically laryngeal organ-preservation therapies, have been hampered by the lack of a well-validated instrument and have not been reported.

Recently, a head and neck cancer–specific quality-of-life instrument (HNQOL) has been developed and validated.[5] It consists of 20 questions on head and neck cancer symptoms that generate scores for 4 domains or dimensions of quality of life: communication, eating, pain, and emotional well-being. Global symptoms, disability attributable to head and neck cancer, and response to treatment are also assessed. Each scale of the HNQOL has been validated for test-retest reliability and for construct valid-

METHODS

After VA research committee and human studies approval were obtained, the Hines VA Cooperative Studies Program Coordinating Center identified a total of 93 living patients who were participants in the VA Laryngeal Cancer Study No. 268. Several quality-of-life outcomes measures were mailed to these patients. The instruments included the SF-36 general health status measure,[6] the HNQOL,[5] a short smoking and alcohol use questionnaire, and the Beck Depression Inventory (BDI).[7] Information on smoking and alcohol use and the BDI had been collected before treatment and was measured serially in this trial and is included with these new data. Initial nonresponders were sent second questionnaires if new addresses could be identified. Patients' responses were entered into a database, checked, and then transferred to the Hines VA Cooperative Studies Program Coordinating Center database to be analyzed with initial and follow-up data from the VA study No. 268.

Baseline demographics and clinical characteristics including age, sex, tumor TNM stage, Karnofsky status, race, occupation, and level of education were obtained from the original data set. Two comparisons were made between 2 groups. The patients initially randomized to the surgery and RT group were compared with patients randomized to the induction CT + RT group. Also patients who had successful organ preservation (CT + RT with larynx) were compared with patients who underwent laryngectomy (either planned surgery and RT or salvage laryngectomy after unsuccessful CT + RT). Baseline demographics, clinical characteristics, and quality-of-life outcomes were analyzed using parametric statistical methods. Categorical and continuous measures were compared between groups using the χ^2 test and the Student t test, respectively. Comparisons before and after treatment within patients were completed using a paired t test. A 2-sided α level of .05 was considered statistically significant.

THE SF-36 GENERAL HEALTH MEASURE

General health status was measured using the SF-36 general health measure. The SF-36 is a commonly used, well-validated, general health measure that generates scores for 8 domains: physical functioning (PF), role limitations attributable to physical problems (RP), bodily pain (BP), general health perception (GH), vitality (VT), social functioning (SF), role limitations because of emotional problems (RE), and mental health (MH) (**Table 1**). Scoring algorithms, population norms, and cross-disease scores are available from Medical Outcomes Studies literature and reference manuals.[6] The SF-36 takes about 10 to 15 minutes to complete.

HNQOL INSTRUMENT

Head and neck cancer–specific quality of life was measured using the HNQOL, a validated instrument that generates scores for 4 domains: communication, eating, head and neck pain, and emotional factors that are specific for patients with head and neck cancer.[5] Normative data for a population of 397 patients with head and neck cancer have been previously reported.[8] Published scoring algorithms were used to calculate the HNQOL domain scores, which are on a scale similar to the SF-36, with 0 the worst possible score and 100 the best. The HNQOL also generates a global or overall bother score for symptoms related to patients' head and neck cancer condition, and a score for the patients' assessment of their response to treatment, both with 100 as the best score.

BECK DEPRESSION INVENTORY

The BDI,[7] a 13-item instrument completed before and after treatment by the VA Laryngeal Cancer Study participants, was used to assess patients' symptoms of depression. Scoring of the BDI was performed by summing the individual items. Missing items were assigned a value that was the mean score of the other individual items. Published criteria for assigning the degree of depression were used with scores of 0 to 3 for minimal depression, 4 to 7 for mild, 8 to 15 for moderate, and 16 or greater indicative of severe depression. For analysis of the data, patients with minimal or mild depression (scores 0-7) were grouped as no depression, and patients with moderate or severe depression (scores $\geq$8) were grouped as with depression. Before treatment vs after treatment rates of depression for each group were calculated and compared.

ALCOHOL AND SMOKING

Smoking status was assessed by one question, which classified patients as to whether they currently were not smoking or smoked less than 1 cigarette a day, 1 to 9, 10 to 19, 20 to 30, or more than 30 cigarettes a day. Use of alcohol was assessed by asking how many days a week, on average, patients had any alcohol. Those who drank alcohol were asked to quantitate how many drinks a day they had. Drinking status was classified at risk or not at risk using a standard classification scheme that takes into account age, sex, frequency, and volume of alcohol consumed. Patients at risk were defined as men 64 years or younger who consumed on average 15 or more drinks per week; men 65 years or older who consumed 8 or more drinks per week; or women who consumed 8 or more drinks per week.[9]

CURRENT LARYNX STATUS AND SPEECH INFORMATION

To be sure patients had not had a laryngectomy since the end of the VA study No. 268 data collection, patients were asked if they had undergone laryngectomy. Patients who underwent laryngectomy were asked what type of artificial voice they most often used: esophageal speech, electrolarynx, tracheoesophageal speech, no artificial voice, or other means of communication. Patients were also queried on whether they had a tracheotomy tube or gastrostomy or feeding tube in place.

ity. The HNQOL addresses all major issues that would seem important for assessment of the VA Laryngeal Cancer Study patients, especially when coupled with a general health survey instrument such as the 8-domain Medical Outcomes Studies Short-Form 36 (SF-36) instrument.[6]

The VA Laryngeal Cancer Study offers a unique opportunity to assess the quality of life aspect of organ-

Table 1. Domains of the Short-Form 36 General Health Measure*

Domain	Meaning of Score
Physical functioning (PF)	Limitations in performing various physical activities
Role physical (RP)	Problems with work or other daily activities as a result of physical health
Bodily pain (BP)	Extent of pain or limitations due to pain
General health (GH)	Perception of personal health
Vitality (VT)	Level of energy
Social functioning (SF)	Extent and frequency of interference with social activities due to physical and emotional problems
Role emotional (RE)	Problems with work or other activities due to emotional problems
Mental health (MH)	Feelings of nervousness and depression

**Scores standardized with 0 indicating worst and 100, best score.*

preservation therapy since the argument of quantity of life vs quality of life tradeoffs is not particularly pertinent. Quantity of life, as measured by survival, was similar between the 2 treatment groups. In addition, patients were randomized between organ preservation and traditional surgery and RT treatments, thus minimizing selection bias. This study was undertaken to assess the long-term quality of life in patients with advanced laryngeal cancer in the VA randomized trial using patient-oriented, health status assessment instruments, including a disease-specific quality-of-life instrument, the HNQOL.

RESULTS

BASELINE DEMOGRAPHICS

Of the initial group of 93 known survivors from 1995 follow-up data, 17 additional patients had died in the subsequent 2 years. Of the 76 remaining patients, 11 had no known address or telephone number, 2 refused to answer the survey, and 17 did not respond to the surveys. Forty-six (71%) of 65 patients who could be reached completed the surveys, 25 who were in the surgery and RT arm, and 21 originally assigned to the chemoradiation arm. Nonresponders were evenly distributed by initial randomization (9 from the laryngectomy and RT, and 10 from the CT + RT group), and distributed between patients who had laryngectomy (12 patients) vs organ preservation (7 patients) as would be expected. The mean length of follow-up for the 46 patients was 10.4 years (range, 8.5-12.7 years).

Baseline demographics and clinical characteristics including age (mean age, 58.3 years for whole group), sex (42 [91.3%] were men), tumor TNM stage, Karnofsky status, race, occupation, and level of education are presented in **Table 2**. There were no statistical differences between the survivors randomized to surgery vs chemoradiation with the exception of age, for which the CT patients were significantly older (mean age, 61.2 years) than those randomized to surgery (mean age, 55.7 years). When the patients who had undergone laryngectomy were compared with those who had not, there were no differences in baseline demographics, original tumor classification, or performance status (Table 2). Additional analysis comparing groups based on T2/T3 vs T4 tumors demonstrated no significant differences between groups based on original randomization or laryngectomy status.

HEALTH STATUS OF ALL PATIENTS IN THE STUDY

Compared with the US male population norms, the patients with laryngeal cancer had significantly lower ($P<.05$) scores on all domains except the BP domain of the SF-36. Most dramatic differences were seen in the PF, RP, and RE domains of the SF-36, each of which was more than 20 points lower in the patients with laryngeal cancer (**Figure 1**).

QUALITY-OF-LIFE COMPARISONS OF PATIENTS RANDOMIZED TO SURGERY AND RADIATION VS CHEMORADIATION ARMS

Although patients in the group randomized to chemoradiation (n = 21) had better scores on all domains of the SF-36 compared with patients who were randomized to laryngectomy and RT, only scores on the MH domain for the CT group (76.0) were statistically better ($P<.05$) than the surgery and RT group (63.0) (**Figure 2**). The group randomized to CT also had significantly better scores on the HNQOL pain domain (81.3) compared with the laryngectomy and RT group (64.3; $P<.05$). When compared with patients originally randomized to surgery and RT, the patients randomized to the chemoradiation group tended to have better scores on the eating and emotion domain of the HNQOL, but these were not statistically significant ($P>.05$) (**Figure 3**).

Only 2 (10%) of 21 patients randomized to the surgical arm of the study for whom BDI data were available were moderately or severely depressed before treatment, while after treatment 7 (28%) of 25 patients had moderate or severe depression (scores >8 on the BDI). In the group that received chemoradiation, 2 (11%) of 18 were depressed before treatment, and 3 (15%) of 20 were depressed in this long-term assessment.

QUALITY OF LIFE IN PATIENTS WHO HAD SUCCESSFUL ORGAN PRESERVATION VS PATIENTS WHO UNDERWENT LARYNGECTOMY

Patients who had successful organ preservation (CT + RT with larynx) tended to have better scores on all domains of the SF-36 when compared with patients who had undergone laryngectomy (either surgery and RT or salvage laryngectomy after CT + RT) (**Figure 4**). Specifically, patients who had not undergone laryngectomy scored significantly higher on the BP domain (88.5) of the SF-36 than the laryngectomy group (56.5; $P<.001$), and scored significantly higher on the MH (79.8) than the laryngectomy group (64.7; $P<.05$). Patients with intact larynges had statistically better scores on the emotion domain (89.7; $P = .05$) and their impression of their response to treatment (86.5; $P = .005$) on the HNQOL

Table 2. Baseline Demographics and Clinical Characteristics of Patients by Randomization*

Characteristics	Surgery + RT	CT + RT	No Laryngectomy	Laryngectomy	Overall
Mean age, y	55.7	61.2†	56.5	58.9	58.3
No. of patients	25	21	13	33	46
Tumor stage					
1	1 (4)	0 (0)	0 (0)	1 (3)	1 (2)
2	3 (12)	1 (5)	1 (8)	3 (9)	4 (9)
3	13 (52)	15 (71)	11 (85)	17 (52)	28 (61)
4	8 (32)	5 (24)	1 (8)	12 (36)	13 (28)
Node stage					
0	13 (52)	12 (57)	5 (38)	20 (61)	25 (54)
1	5 (20)	3 (14)	4 (31)	4 (12)	8 (17)
2	5 (20)	4 (19)	3 (23)	6 (18)	9 (20)
3	2 (8)	2 (10)	1 (8)	3 (9)	4 (9)
Stage					
III	11 (44)	12 (57)	8 (62)	15 (45)	23 (50)
IV	14 (56)	9 (43)	5 (38)	18 (55)	23 (50)
Performance status					
60	1 (4)	1 (5)	0 (0)	2 (6)	2 (4)
70	6 (24)	1 (5)	0 (0)	7 (21)	7 (15)
80	5 (20)	3 (14)	4 (31)	4 (12)	8 (17)
90	11 (44)	11 (52)	5 (38)	17 (52)	22 (48)
100	2 (8)	5 (24)	4 (31)	3 (9)	7 (15)
Mean Karnofsky performance status	82.8	88.6	90	83.6	85.4

*Values are number (percentage) except where otherwise noted. RT indicates radiation therapy; CT, chemotherapy.
†P<.05 for comparisons between surgery and RT vs CT + RT or between laryngectomy and no laryngectomy.

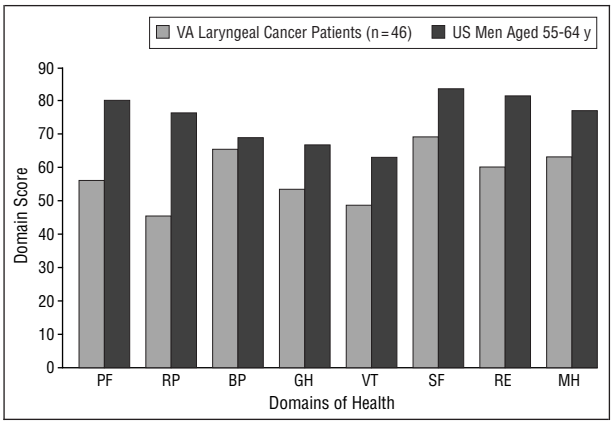

Figure 1. *Comparison of health-related quality of life for patients with head and neck cancer vs US men aged 55 to 64 years using the domains of the Medical Outcomes Studies Short-Form 36 instrument. PF indicates physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; and MH, mental health. P<.05 for all domain differences with the exception of BP.*

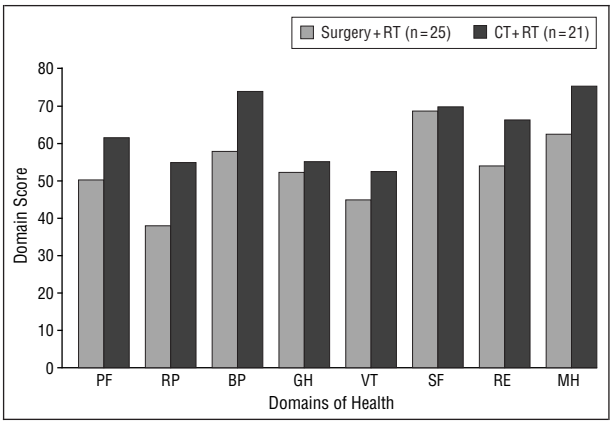

Figure 2. *Comparison of health status for surgery and radiation therapy (RT) vs chemotherapy (CT) + RT patients for domains of the Medical Outcomes Studies Short-Form 36 instrument (see legend to Figure 1 for domains and expansion of abbreviations). P<.05 for mental health.*

than the patients who underwent laryngectomies who scored 79.4 and 70.3, respectively, on the emotion domain and response to treatment item (**Figure 5**). Of patients with successful organ preservation, before treatment BDI scores were less than 8 in only 1 (8.3%) of 12 evaluable patients, and 1 (7.7%) of 13 patients at this long-term assessment. Of the laryngectomy group, 3 (11%) of 27 evaluable patients scored poorly (>8) on the BDI before treatment, and 9 (28%) of 32 were depressed at long-term follow-up. Of all the study patients evaluable at long-term follow-up, 10 (22.2%) of 45 patients had BDI scores consistent with moderate or severe depression. Nine of those 10 had undergone laryngectomies.

SMOKING

A total of 45 (98%) of 46 patients had used tobacco before entry into the VA study No. 268. Eight (17%) of 46 patients in this study reported smoking within the year before this assessment, more than half of whom smoked more than a pack a day. Six (46%) of 13 patients with preserved larynges continued to smoke compared with 2 (6%) of 33 who had undergone laryngectomy ($P<.001$). At randomization into the initial study, 38 (83%) of 46 patients reported using alcohol, while at this long-term assessment, 20 (43%) of these same 46 patients reported drinking any alcohol, and 11 (55%) of these 20 patients drank enough to be considered at risk for additional alcohol-related illnesses.[9]

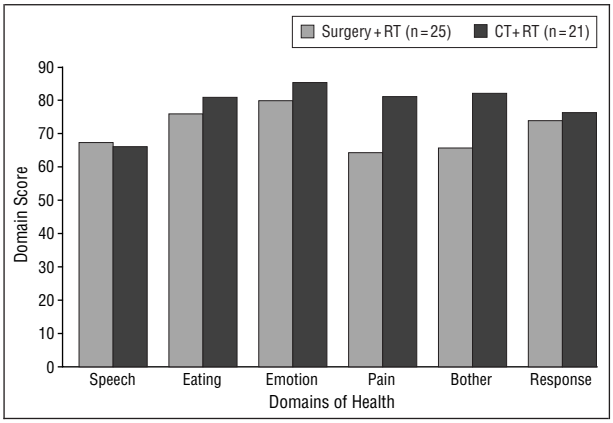

Figure 3. *Comparison of health status for surgery and radiation therapy (RT) vs chemotherapy (CT) + RT patients for 6 domains of the Head and Neck Quality of Life (HNQOL) instrument. Response indicates the treatment item of HNQOL; bother, the overall bother item on the HNQOL.* P<.05 *for pain.*

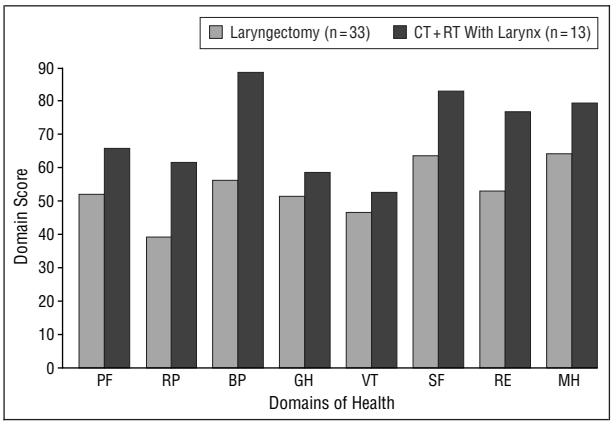

Figure 4. *Comparison of health status for laryngectomy vs no laryngectomy patients for domains of the Medical Outcomes Studies Short-Form 36 instrument (see legend to Figure 1 for expansion of abbreviations). CT indicates chemotherapy; RT, radiation.* P<.05 *for BP and MH.*

COMMENT

GENERAL HEALTH STATUS

Assessment of quality of life in long-term survivors of the VA Laryngeal Cancer Study population demonstrated that, as a group, surviving patients who were randomized to the chemoradiation arm of the study tended to have better health-related quality-of-life scores on the SF-36 than patients who were randomized to laryngectomy and RT. Although scores were significant at $P<.05$ for only the SF-36 MH domain and the HNQOL pain domain, there was more than a 10-point difference in the PF, RP, BP, and RE domains of the SF-36, and more than a 15-point difference in patients' overall complaints due to their head and neck condition or treatment now more than 10 years after treatment.

When compared with the US male population aged 55 to 64 years, patients with laryngeal cancer had significantly worse scores on all domains of the SF-36 except BP, which did not reach significance. Patients who had successful organ preservation (n = 13) had the highest SF-36 and HNQOL domain scores of any of the 4 groups analyzed. Patients with intact larynges had significantly better BP scores, but otherwise had similar SF-36 domain scores on the other 7 domains of general health compared with their US male counterparts (**Figure 6**). Their scores on the SF, RE, and MH were similar to the US male population, suggesting that patients with intact larynges (1) did not experience more problems with work or other daily activities because of emotional problems, (2) did not have more problems with social activities because of physical and emotional conditions, and (3) did not have more feelings of nervousness or depression than the US male population aged 55 to 64 years.

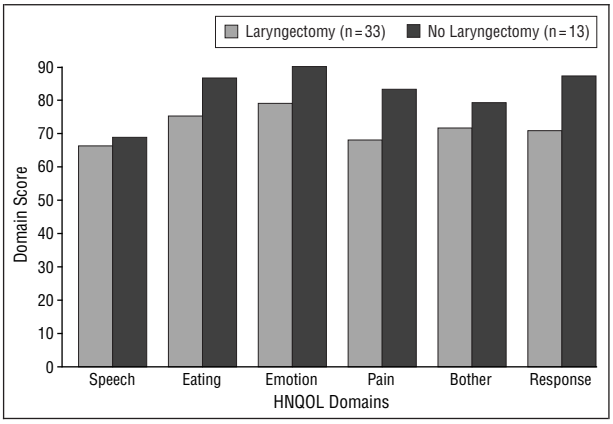

Figure 5. *Comparison of health status for laryngectomy vs no laryngectomy patients for 4 domains of the Head and Neck Quality of Life (HNQOL) instrument: bother (overall bother from HNQOL) and response (response to treatment item from HNQOL).*

In contrast, the laryngectomy group had significantly lower mean scores on all domains of the SF-36 when compared with US males aged 55 to 64 years (**Figure 7**). When compared with patients with intact larynges, patients who underwent laryngectomy scored more than 10 points lower on the PF and MH domains; 20 or more points worse on the RP, SF, and RE domains; and more than 30 points lower on the BP domain of the SF-36 (Figure 4). These differences reached statistical significance ($P<.05$) only for the BP and MH domains, probably due to the decreased power to detect differences in scores resulting from a small sample size (n = 13) of long-term organ-preservation patients in this study. Nevertheless, all the trends demonstrate that patients with intact larynges tend to have not only better disease-specific quality-of-life scores but also better general health status.

SPEECH

We initially thought that patients in the laryngectomy and RT group in the study would be substantially more bothered by speech or communication problems. In fact, the speech scores on the HNQOL survey for the chemoradiation group were similar to the speech scores in the laryngectomy group. It was conceivable that the speech scores were similar in the chemoradiation group because 8 patients in this group had salvage laryngectomy and their scores may have lowered the mean speech score. However, when the analysis was performed based on laryngectomy or no laryngectomy status, the mean speech

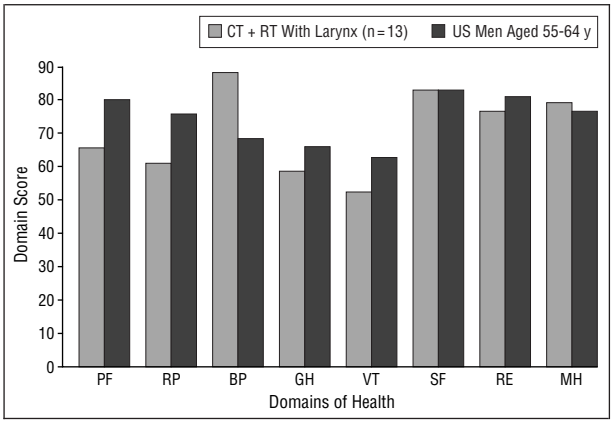

Figure 6. *Comparison of health-related quality of life for laryngeal-preservation patients vs US men aged 55 to 64 years using the domains of the Medical Outcomes Studies Short-Form 36 instrument (see legend to Figure 1 for expansion of abbreviations). CT indicates chemotherapy; RT, radiation therapy.* P<*.05 for BP only, which was better than US population group.*

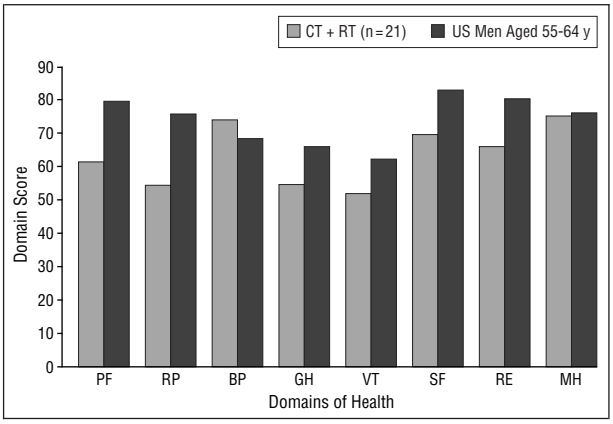

Figure 7. *Comparison of health-related quality of life for chemotherapy (CT) and radiation therapy (RT) patients vs US men aged 55 to 64 years using the domains of the Medical Outcomes Studies Short-Form 36 instrument (see legend to Figure 1 for expansion of abbreviations).* P<*.05 for PF and RP.*

domain score for the patients who had successful organ preservation was still similar to the mean speech score for patients who underwent laryngectomy.

These findings may be explained in part by several factors. Most of the patients who underwent laryngectomy (30/33) were using some means of artificial voice that allowed them to communicate reasonably well. All patients who underwent long-term laryngectomy have had substantial time to readjust to their new condition; therefore, their scores may be higher because they are less bothered by any difficulties with volume, clarity, or overall ability to speak. Finally, speech differences might be minimal because both the laryngectomy and the organ-preservation groups could have substantial problems with voice. The latter theory could be supported by the finding that all the laryngeal cancer groups had mean communication scores substantially worse than communication scores of patients with head and neck tumors at other sites that would be less likely to affect speech. In the original report of the HNQOL instrument,[5] we described 51 patients with tumors of the head and neck that did not involve the oral cavity, pharynx, or larynx whose mean communication scores were substantially higher (85.4) than any of those with organ preservation or patients who underwent laryngectomy.

The results of the current study extend the earlier analysis of communication scores from the 2-year survivors of the VA larynx cancer trial.[10] Hillman et al[10] found that, at 24 months, technician-assessed intelligibility scores from audio recordings were 95.8% for the organ-preservation group, 90.8% for the chemoradiation group, and 84.9% for the surgery and RT group. A 24-item patient-assessed communication profile showed a similar 5% point spread of scores between groups. There are several reasons why there may be detectable differences in patient-assessed speech performance at 24 months and not at this follow-up, now 10 or more years after treatment. There may be a survivor effect, that is, the 10-year survivors are doing better than the group who had survived 2 years. There may have been adjustments in patients' expectations, so that they have adjusted to and are less bothered by any speech problems. Patients may indeed be speaking better at 10 years than at 2 years because of practice. In addition, the instruments may be measuring different constructs. For instance, the 24-item communication profile used at baseline and 2 years seems to have the potential to measure levels of depression and avoidance behavior, so that differences in scores may be confounded and reflect differences in degrees of depression (that were found in this study) as well as differences in speech production. Finally, the 4-item speech domain of the HNQOL may not be sensitive enough to detect real differences in speech function with this sample size. However, the instrument has been shown to discriminate between other groups of patients with head and neck cancer and seems to have good face validity for assessing communication levels in patients treated for laryngeal cancer.[5]

When patients who had long-term successful organ preservation were compared with patients who underwent laryngectomy, it was notable that there were smaller differences in the HNQOL speech domain scores than there were differences in BP, head and neck pain, or emotional well-being. This supports the study of Mohide et al,[11] who found that patients who underwent laryngectomy are more concerned with physical consequences of surgery and interference with social activities than impaired communication. Our results also support the impression of DeSanto et al[12] that patients who underwent laryngectomy are more bothered by physical consequences such as a stoma than they are by voice alteration.

Finally, these data on speech quality after treatment of advanced laryngeal cancer provide a new perspective about speech difficulties after treatment for advanced laryngeal cancer. These new long-term, patient-oriented data on speech production after laryngectomy would seem to challenge the validity of the assumptions in the classic article by McNeil et al[13] on time tradeoffs for patients with laryngeal cancer, in which it was reported that some patients would tradeoff a significant quantity of life because of expected decrements in quality of life associated with laryngeal speech. Over the long-term, it seems that VA patients who underwent laryngectomy and speech rehabilitation have, by their

own assessment, compensated better than many may have predicted.

MENTAL HEALTH

Several authors[11,12,14-16] have described the impact of head and neck cancer and laryngectomy on SF, emotional well-being, and MH. It is possible that organ-preservation therapies may improve outcomes in these domains of health. In this study, the chemoradiation group had significantly better mean scores on the SF-36 MH domain (76.0) than the laryngectomy and RT group (63.0). Because the MH domain measures both anxiety and depression, it is difficult to know if patients experienced more problems with anxiety or depression components of the SF-36 MH scale, but analysis of the BDI data would suggest that depression is a significant problem, especially in patients who had undergone laryngectomy. While only 1 (8%) of 13 patients with successful organ preservation had long-term BDI scores that were moderate or severe (defined as scores >8), 9 (28%) of 32 patients who had initial or salvage laryngectomy had depression scores indicative of moderate depression. The emotional impact of treatment for these advanced laryngeal cancers was also assessed with the RE domain of the SF-36, as well as the emotional domain of the HNQOL, which queries patients about potential embarrassment regarding their condition, concerns about appearance, emotional problems, financial worries, worries that their condition will get worse, or frustration about their head and neck condition. Again, although there were no statistical differences, patients randomized in the organ-preservation group tended to have higher RE scores (66.7) and HNQOL emotion domain scores (85.7) than patients in the surgical group, who scored 54.7 on the RE and 79.5 on the RE domain of the HNQOL. When the analysis was performed by laryngectomy status, emotion scores of the SF-36 were markedly better in the organ-preservation patients (76.9) than in the laryngectomy patients (53.5), and HNQOL emotion domain scores were statistically higher in the organ-preservation group (89.7) than in the laryngectomy group (79.4). These findings suggest that patients with organ preservation have considerably fewer problems with work or other daily activities as a result of emotional problems, and specifically that their head and neck cancer–related emotional issues are substantially less problematic. These results are consistent with the BDI analysis.

PAIN

Although patients' perceptions of their response to therapy were similar, patients who were randomized to the surgery and RT arm of the study were much more bothered by their head and neck condition or treatment than patients in the chemoradiation arm of the study (Figure 3). Chronic pain is not uncommon in patients with head and neck cancer. The physical sequelae and shoulder pain that result from resection of the spinal accessory nerve during neck dissection have been well described.[17] Previous studies[8] have shown that patients' overall discomfort correlates well with the HNQOL pain domain scores. Interestingly, in this study, patients who underwent laryngectomy (most of whom also had neck dissections) had dramatically low ($P<.05$) BP scores on the SF-36 compared with US men aged 55 to 64 years, indicating a great degree of pain or limitations because of pain. Whether this pain can be attributed to their head and neck treatment alone, or other comorbid conditions, is unknown since a detailed comorbidity assessment was not performed when the original study was undertaken, and patient-reported comorbidity assessment was not undertaken as part of this survey. It is possible that some of the BP scores may be related to the lower initial Karnofsky status of the surgical patients, although the Karnofsky differences were small and not statistically significant. Nevertheless, pain scores on the HNQOL were considerably lower in the group randomized to surgery and in the laryngectomy group, suggesting that head- and neck-associated discomfort plays an important role in patients' quality of life after laryngectomy and, in the long-term, may be as important as speech differences when comparing quality of life between laryngectomy and organ-preservation patients.

EATING

The HNQOL eating domain assesses problems with chewing, dryness, taste, swallowing solids and liquids, and trismus. We suspect that differences in eating scores between groups were not larger because many of the symptoms assessed on the eating domain (ie, denture and chewing problems, RT-induced xerostomia and burning, and trismus) are associated with RT, common to both randomized groups of patients. We expected that although the laryngectomy group may have scored low on 2 of the eating domain questions (problems with swallowing soft foods/solids and problems with taste), the magnitude of problems with these symptoms may have been insufficient to show any significant differences on this domain with this sample size. In fact, only 1 of the patients in this study (a patient randomized initially to surgery and RT) currently uses a gastrostomy tube, supporting the idea that most patients are at least swallowing soft foods or liquids.

SMOKING AND USE OF ALCOHOL

Counseling about smoking cessation and alcohol use/abuse must continue to be a priority for head and neck oncologists. It has been shown that smoking and alcohol consumption are independent risk factors for head and neck cancer, and that combined they have a synergistic or multiplicative effect rather than an additive effect.[18] Moreover, continued smoking and drinking after the first diagnosis of head and neck cancer significantly increase the likelihood of developing a second malignancy and adversely affect survival after the occurrence of a second cancer.[19] Experts on smoking cessation have recognized the importance of a "teachable moment," such as a new diagnosis of a myocardial infarction or head and neck cancer,[20] as a particularly effective time for cessation teaching. However, when Fabian et al[21] questioned 134 patients, only 20 (14.9%) were aware of the causative factors of oral cancer.

Although smoking rates in the VA study[21] dropped from 98% to 17%, cessation seems to be mostly related to laryngectomy status. Forty-six percent of patients with intact larynges continued to smoke, which is higher than the 35% rate for patients with head and neck cancer reported by Ostroff et al.[22] Whether this is related to patient population (motivation to quit), health workers' education efforts, or availability of pharmacological agents cannot be determined. However, with the larger arsenal of medications and counseling currently available to physicians and patients, head and neck oncologists should be prepared to take advantage of this teachable moment and assist patients with their smoking awareness and cessation efforts.

Unfortunately, in this study 83% of patients with laryngeal cancer were drinking alcohol at this long-term follow-up, with most of those drinking enough alcohol to be considered at risk for additional alcohol-related illnesses, including second head and neck cancers. These data seem to underscore the importance of long-term efforts at identifying patients who continue to drink alcohol and persuading them to quit drinking.

Although these long-term quality-of-life data are compelling, they must be interpreted carefully, taking into account the decreased power to detect differences with small sample sizes, the potential for selection biases because the groups followed up are only a fraction of the originally randomized groups, difficulty with assessing comorbid conditions, and statistical error introduced by comparing multiple mean quality-of-life scores. Nevertheless, these data would suggest that the induction CT + RT therapy protocol, which has been demonstrated to have similar survival rates compared with laryngectomy and RT, is also associated with better quality of life for patients. Better quality of life appears to be more related to freedom from pain, better emotional well-being, and lower levels of depression than to preservation of speech function.

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