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HEAD AND NECK ONCOLOGY

W. Derks · J. R. J. de Leeuw · G. J. Hordijk
J. A. M. Winnubst

Reasons for non-standard treatment in elderly patients with advanced head and neck cancer

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Abstract Elderly patients with head and neck cancer are less likely to receive standard treatment. This study assessed the influence that age, tumour characteristics, comorbidity, social support, depressive symptoms and quality of life have on treatment choice. One hundred and five patients between 45 and 60 years of age and 78 patients of ≥70 years of age with carcinoma of the oral cavity (stage ≥II), oro- and hypopharynx (stage ≥II) or larynx (stage ≥III) completed a questionnaire on quality of life (EORTC QLQ-C30 and H&N35), depressive symptoms (CES-D) and social support (RSS12-I). In the 45–60 age group, 89% received standard treatment, compared with 62% of the ≥70 age group. A multivariate logistic regression analysis showed that the following factors predicted non-standard treatment: marital status (widowed), advanced tumour stage, comorbidity, less pain, considering the length of life less important than its quality and old age. This study showed that age itself independently influences treatment choice. However, it should be emphasised that the choice of a treatment should be based on a medical assessment and the patient's preferences, not on chronological age.

Keywords Head and neck neoplasms · Aged · Quality of life · Comorbidity · Therapy

Introduction

The elderly represent the fastest growing segment of the population in western countries. As the number of elderly patients with cancer rises, head and neck surgeons are increasingly faced with a therapeutic dilemma. The disease and its treatment, which is often aggressive, may have a huge impact on the quality of life by affecting the patient's speech, swallowing, and breathing. Various retrospective studies have shown that radical surgery can be performed safely in elderly patients provided there is no severe concomitant morbidity [3, 4, 6, 8, 9, 15, 22]. Our recently published prospective study concerning surgically treated elderly patients is in alignment with these findings [9]. However, as several publications show, standard treatment for head and neck cancer is still less likely in elderly patients [12, 13, 15, 20]. Instead, the elderly are often given less aggressive treatment, and postoperative radiotherapy is frequently withheld. Comorbidity, which increases with age, is thought to play an important role in surgeons' motives to treat the elderly less intensively. Yet as a study of breast cancer patients has shown, even the healthy elderly were less likely to receive standard treatment than younger patients [11]. Other factors that might influence treatment choice are marital status, decreased social support, quality of life and depressive symptoms. Personal opinions held by head and neck surgeons but also by patients and their families can affect treatment choice [16].

Little is known about the factors influencing treatment choice in elderly patients with head and neck cancer. The present study was designed to assess how age, sociodemographic data, comorbidity, social support, depressive symptoms and quality of life influence treatment choice in our clinic.

Subjects and methods

Patients

This study included patients of 70 years and older and patients between 45 and 60 years with newly diagnosed squamous cell carcinoma of the oral cavity (stage ≥II), pharynx (oro- and hypopharynx; stage ≥II), or larynx (stage ≥III) without distant metastasis. These criteria for tumour stage were selected because dilemmas about treatment choice mostly arise in patients with advanced tumours. Between December 1998 and December 2001, 148 patients

W. Derks (✉) · G. J. Hordijk
Department of Otorhinolaryngology,
University Medical Centre Utrecht,
P.O. Box 85500, 3508 GA Utrecht, The Netherlands
Tel.: +31-302506644, Fax: +31-302541922,
e-mail: w.derks@azu.nl

J. R. J. de Leeuw · J. A. M. Winnubst
Research Group Medical and Health Psychology,
University Medical Centre Utrecht, Utrecht, The Netherlands

between the ages of 45 and 60 years and 118 patients aged ≥70 were eligible for this study. The patients were asked to participate in an interview and to answer a questionnaire before treatment. Eleven (4%) patients were excluded due to cognitive impairment, 20 (7%) could not participate because their physical condition had deteriorated, 10 (4%) were missed, and 42 (16%) patients refused to take part. In total 105 (71%) patients in the 45–60 age group and 78 (66%) patients of ≥70 years of age took part in the study.

Methods

All patients were treated at the University Medical Centre Utrecht, The Netherlands. The tumour stage at the time of initial diagnosis was classified according to criteria set by the American Joint Committee on Cancer (1992). A treatment proposal was presented at the weekly multidisciplinary tumour conference. In Utrecht, the standard treatment protocol for head and neck cancer is based on guidelines published by the Comprehensive Cancer Centre of the Middle Netherlands (IKMN), stipulating that advanced inoperable tumours must be treated with combined chemoradiotherapy. In our hospital, however, patients over 70 years of age with advanced inoperable tumours receive radiotherapy as standard treatment because of the unacceptable side effects of chemotherapy in this age group. For those who refused to undergo the treatment proposed at the tumour conference, the classification 'patient refusal' was entered.

Every patient's sex, marital status and comorbid conditions were recorded. For those patients who took part in the questionnaire and interview, the following data were also collected: Karnofsky performance status, level of education (five levels) and having children. Comorbidity was classified according to the Kaplan-Feinstein index [14]. The original index was modified to incorporate diabetes mellitus and consists of 13 categories (hypertension, respiratory disease, alcoholism, etc.). All ailments were rated on a scale of 0 to 3. These components were combined to form a 4-point scale (0=no, 1=mild, 2=moderate, 3=severe).

The patients participated in the interview and filled out the questionnaire after the treatment decision was made and before treatment was started. The interview was done by two of the authors (WD or JdL) who were not involved in the decision-making process. The questionnaire contained items about quality of life, depression, social support and trade-offs between quality and length of life.

Quality of life was measured with the European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (QLQ-C30) [1]. This is a general cancer-specific questionnaire consisting of 30 items grouped into five functional scales (physical, role, cognitive, emotional and social functioning), three symptom scales (fatigue, pain and nausea/vomiting), a global quality-of-life scale, and six single questions (dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties).

The EORTC Head and Neck Cancer Quality of Life Questionnaire (H&N35) [5], which was designed for use in combination with the QLQ-C30 questionnaire, consists of six symptom scales (pain, swallowing, senses, speech, social eating and social contacts) and six single items (teeth problems, problems opening the mouth, dry mouth, sticky saliva, cough and feeling ill).

Depressive symptoms were measured with the Centre for Epidemiological Studies Depression Scale (CES-D) [18]. This is a questionnaire of 20 items developed to measure depressive symptoms in the general population. The present study used the total score of the CES-D.

Social support was measured with the short form of the Social Support List-Interactions (RSS12-I) [24]. This is a questionnaire of 12 items developed to measure everyday social support, social support in problem situations and appraisal support (e.g., how often someone receives a compliment) in elderly patients.

Trade-offs between the quality and length of life were measured with the Quality-Quantity questionnaire (QQ questionnaire) [23]. In this eight-item questionnaire, patients have to prioritise statements about quality of life or length of survival.

Statistical analysis

The data were analysed with the statistical packages SPSS 10.0 for Windows and LogXact 2.1. Descriptive statistics and χ^2 tests were used to compare the 45–60 and ≥70 age groups regarding sociodemographic and illness-related characteristics. Student's *t* tests were used to compare the mean scores of the QLQ-C30, H&N35, CES-D, RSS12-I and QQ questionnaires for patients who had received standard or non-standard treatment. A difference of ten points or more on the QLQ-C30 and H&N35 is taken as an indication of clinical significance [17].

Initially, all variables that might influence the treatment choice were examined separately. Asymptotic logistic regression analyses were used for the ≥70 age group. Exact logistic regression analyses were used for the 45–60 age group because of the small number of patients who were given non-standard treatment. Variables that were related to non-standard treatment in the univariate analyses ($P \leq 0.05$) were analysed further with a multivariate logistic regression analysis (taking elderly and younger patients together) using the backward method.

Table 1 Patient characteristics and percentages of the patients receiving non-standard treatment

Patients		45–60 years *n*=148	≥70 years *n*=118	P^1	45–60 years		≥70 years	
					Non-standard[2]	P^3	Non-standard[2]	P^3
Sex	Male	107 (72%)	72 (61%)	*	15%	**	35%	NS
	Female	41 (28%)	46 (39%)		0%		44%	
Marital status	Single	50 (34%)	16 (13%)	**	20%	*	25%	*
	Married	93 (63%)	67 (57%)		7%		33%	
	Widowed	5 (3%)	35 (30%)		0%		54%	
Tumor site	Oral cavity	56 (38%)	58 (49%)	**	9%	NS	38%	NS
	Pharynx	77 (52%)	31 (26%)		13%		52%	
	Larynx	15 (10%)	29 (25%)		7%		24%	
Stage (AJCC)	II	26 (18%)	30 (25%)	NS	12%	NS	40%	*
	III	29 (20%)	31 (26%)		7%		16%	
	IV	93 (63%)	57 (48%)		12%		49%	
Comorbidity	No	47 (32%)	30 (25%)	**	2%	**	13%	**
	Mild	71 (48%)	33 (28%)		7%		27%	
	Moderate	23 (16%)	43 (36%)		26%		51%	
	Severe	7 (5%)	12 (10%)		57%		83%	

[1]χ^2 test: differences between age groups, [2]percentage of the patients not treated with standard treatment, [3]χ^2 test: differences between standard and non-standard treated patients within each age group, *$P \leq 0.05$, **$P \leq 0.01$, NS: not significant

Results

The patient characteristics are shown in Table 1. Sex, marital status, tumour site and comorbidity levels differed significantly between the age groups. The 45–60 age group contained a higher percentage of single patients, and there were more widowed patients in the ≥70 age group. In the elderly age group, fewer patients had a tumour of the pharynx and more had a tumour of the oral cavity. There was more comorbidity in the ≥70 age group. The tumour stage did not differ between the age groups.

The number of patients given non-standard treatment differed significantly between the age groups. In the 45–60 group, 89% received standard treatment in comparison to 62% in the ≥70 age group ($P<0.001$). To find out if treatment choice was different in very old patients, the elderly age group was subdivided into two categories: 70–79 and ≥80 years of age (Table 2). Standard treatment was performed in only 36% of the patients of 80 years and older, while 18% of the octogenarians received no treatment at all. In the ≥80 age group, postoperative radiotherapy was more frequently withheld, and limited surgery was performed more often than in the other age groups. In the 45–60 and 70–79 age groups, 3 and 9% of the patients refused standard treatment, compared to 18% of the patients in the ≥80 age group.

In Table 1 the percentages of non-standard treatment in relation to sex, marital status, tumour site, stage, and comorbidity are listed. In the 45–60 age group, significantly

Table 2 Standard treatment and non-standard treatment in different age groups

Patients	45–60 yr *n*=148	70–79 yr *n*=79	≥80 yr *n*=39
Standard treatment	132 (89%)	59 (75%)	14 (36%)
Non-standard treatment	16 (11%)	20 (25%)	25 (64%)
No treatment	6 (4%)	10 (13%)	7 (18%)
No surgery but (chemo)radiotherapy	6 (4%)	4 (5%)	4 (10%)
Limited surgery	2 (1%)	2 (2%)	8 (21%)
No postoperative radiotherapy	0 (0%)	4 (5%)	6 (15%)
Radiotherapy instead of combined chemo/radiotherapy	2 (1%)	N/A	N/A
Patient refuses standard treatment	5 (3%)	7 (9%)	7 (18%)

Table 3 Comparison of the questionnaire data for elderly and younger patients receiving standard and non-standard treatment

Patients	45–60 years[1]		≥70 years[1]	
	Standard *n*=98	Non-standard *n*=7	Standard *n*=54	Non-standard *n*=24
EORTC QLQ-C30				
Physical functioning	80	57	73	57*
Social functioning	82	67	79	86
Role functioning	78	59	72	77
Emotional functioning	68	54	65	72
Cognitive functioning	84	69	80	85
Quality of life	61	52	61	58
Fatigue	32	44	28	33
Nausea and vomiting	6	10	4	7
Pain	31	24	32	18*
EORTC H&N35				
Pain	38	55	40	35
Swallowing	29	50	24	24
Senses (taste/smell)	11	14	14	15
Speech	20	30	27	20
Social contact	7	21	8	15
Social feeding	22	36	21	25
Social support				
Daily social support	11.2	11.2	11.3	10.2
Support in problem situations	11.2	11.4	11.4	9.9
Appraisal support	10.4	10.7	10.7	8.6*
CES-D	13	21	14.1	13.1
QQ questionnaire				
Quality of life	13	12	13.8	15.3
Length of survival	14	13	13.7	10.0**

[1]Student's *t* test, *$P\leq0.05$, **$P\leq0.01$

more single patients did not receive standard treatment; in the elderly age group, non-standard treatment was given more often to widowed persons. Among patients aged ≥70, stage III tumours were treated significantly more frequently by standard treatment than stage II and IV tumours. In neither age group were there significant differences in tumour site. In both groups, a higher level of comorbidity was related to a larger percentage of non-standard treatment. Moreover, 13% of the elderly without comorbidity and 27% with mild comorbidity did not receive standard treatment; by comparison, in the 45–60 age group 2% of the patients without and 7% with mild comorbidity were not given standard treatment.

Table 4 Prognostic factors for non-standard treatment (univariate analyses)

Age Standard/non-standard treatment	45–60 years[1] 98/7	≥70 years[2] 54/24
Tumor characteristics		
Site (oral cavity, pharynx, larynx)	NS	*
Stage (II, III, IV)	NS	*
Sociodemographic factors		
Age	–	**
Sex	NS	NS
Marital status (single, widowed, married)	NS	*
Having children	NS	NS
Level of education (5 levels)	NS	NS
General health status		
Karnofsky performance status	*	NS
Comorbidity (Kaplan-Feinstein)	*	*
EORTC QLQ-C30		
Physical functioning	*	*
Social functioning	NS	NS
Role functioning	NS	NS
Emotional functioning	NS	NS
Cognitive functioning	NS	NS
Quality of life	NS	NS
Fatigue	NS	NS
Nausea and vomiting	NS	NS
Pain	NS	*
EORTC H&N35		
Social contacts	*	NS
Social feeding	NS	NS
Pain	NS	NS
Swallowing	NS	NS
Senses (taste/smell)	NS	NS
Speech	NS	NS
Social support		
Daily social support	NS	NS
Support in problem situations	NS	NS
Appraisal support	NS	**
CES-D	*	NS
QQ questionnaire		
Quality of life	NS	NS
Length of survival	NS	**

[1]Exact logistic regression analyses, [2] asymptotic logistic regression analyses (likelihood ratio test), *$P \leq 0.05$, **$P \leq 0.01$, NS: not significant

The data from the questionnaire are presented in Table 3. Elderly patients not receiving standard treatment scored significantly worse on physical functioning. Moreover, they reported significantly less pain on the QLQ-C30 than the elderly who were receiving standard treatment. Whether given standard or non-standard treatment, the elderly did not differ significantly on the other variables of the QLQ-C30, H&N35 and CES-D. Elderly patients given non-standard treatment received significantly less appraisal support. In addition, compared to the elderly who received standard treatment, they did not give longevity as much importance. Only seven patients in the 45–60 age group did not receive standard treatment; therefore, the differences would have to be very great to be significant. Younger patients given non-standard treatment scored worse on most variables of the QLQ-C30 and H&N35. Differences of more than ten points were found for physical, social, role, emotional and cognitive functioning, fatigue, pain (H&N35), swallowing, speech, social contacts and social feeding. Also, the total score of the CES-D is high in comparison to that of younger patients receiving standard treatment.

Univariate logistic regression analyses (Table 4) were performed on the data for the patients who answered the questionnaire. In the ≥70 age group, the following factors were predictive for receiving non-standard treatment: old age, tumour stage (IV), tumour site (pharynx), marital status (widowed), more comorbidity, poor physical functioning, less pain, less appraisal support and giving longer life less priority. In the 45–60 age group, non-standard treatment was associated with more comorbidity, a lower Karnofsky performance score, poor physical functioning, more problems with social contacts and more depressive symptoms. All significant variables of the univariate analyses were analysed in a multivariate logistic regression analysis of both age groups combined. The purpose of the analysis was to determine whether age was an independent predictor of treatment choice. When corrected for each other, the factors that predicted non-standard treatment significantly were marital state (widowed), tumour stage (IV), comorbidity, less pain, considering length of life less important and old age.

Discussion

This is one of the first studies designed to evaluate the influence of age, comorbidity and other factors such as social support and quality of life on treatment choice in elderly patients with advanced head and neck cancer. In the present study, patients of 70 years and older received standard treatment less often than younger patients. In the subgroup of patients of 80 years and older this percentage was even higher. These findings are in agreement with several retrospective head and neck cancer studies [12, 13, 5, 20]. As the medical literature does not give a clear definition of being 'aged', we set the cut-off point at 70 years. Although this point is used frequently [12, 15], some authors have selected an older [8, 20] or younger age limit [2, 19].

We decided to take the age of 60 as the upper limit for the control group instead of using a continuous cohort to enhance the possibility to find differences between elderly and middle-aged patients.

Elderly patients with head and neck cancer differ from younger ones. As expected, elderly patients had more comorbidity and were more often widowed. Because women have a longer life expectancy, the study population included more women in the ≥70 age group [7, 20]. Fewer elderly patients had cancer of the pharynx, whereas more had cancer of the oral cavity. The numbers in this study are small. However, this different tumour distribution in elderly patients is also found in other studies [20].

In agreement with other studies, we found that a higher comorbidity index and poor physical functioning were associated with non-standard treatment [7, 8]. However, even when the comorbidity level was equal, patients of 70 years and older received standard treatment less often. Several authors studying cancer in other patient groups also mentioned that the effect of age on treatment choice remained intact after correction for comorbidity [10, 11]. Patients who reported more pain on the QLQ-C30 received standard treatment more frequently. Nonetheless, pain symptoms measured with the H&N35 had no predictive value for non-standard treatment. This pain scale is only concerned with pain at specific tumour sites, whereas other kinds of pain are not represented. This might explain the difference.

Social factors were also predictive for non-standard treatment. Elderly patients reporting less appraisal support and younger patients who had more problems with social contacts (H&N35) received standard treatment less often. This suggests that patients lacking a close social network are more afraid to undergo major treatment; it might also suggest that the surgeon is less likely to recommend it. Other instruments measuring social functioning, like the QLQ-C30 social functioning scale, were not associated with a greater risk of non-standard treatment. Remarkably, widowed persons were more often not treated according to the standard protocol. This is in agreement with the findings from a breast cancer study [21], which suggested that older unmarried women were more concerned than married women about treatment-related problems after surgery. Considering the 45–60 age group, the factors of sex (male) and marital status (single) showed no predictive value in the exact logistic regression analysis. This is in contrast to the results presented in Table 3 and may be explained by the small number (n=7) of younger patients receiving non-standard treatment who answered the questionnaire.

Logistic regression analysis showed that in the ≥70 age group, tumour site (pharynx) and stage (IV) were predictive for non-standard treatment. In the elderly age group, stage III tumours were more often treated by standard means than stage II tumours. This difference is largely due to the exclusion of stage II laryngeal tumours. Radiotherapy is standard treatment for most stage III laryngeal tumours, and not receiving standard treatment is less often seen with radiotherapy than with surgery.

The choice of a treatment was also influenced by the preferences of the elderly patients. The QQ questionnaire showed that elderly patients who gave length of life less priority more often received non-standard treatment. This is in accordance with a study demonstrating that older patients want to have a greater survival advantage before they would choose a toxic regimen over a less toxic alternative [25]. We found that 18% of the patients in the ≥80 age group refused the treatment proposal of their head and neck surgeon. A retrospective head and neck cancer study also noted that elderly patients and their families refused invasive treatment more frequently [12]. However, a breast cancer study concluded that patient and family preferences had hardly any influence on treatment choice [21]. Other studies showed that personal opinions of head and neck surgeons can also affect treatment choice. For example, as a general cancer study has shown, physicians assume that the expected quality of life after treatment is more important to elderly patients than a longer survival time [16].

A confounder in this study might be that the patients who answered the questionnaire were in better health. In comparison with non-participants, they had less comorbidity and received standard treatment more often. However, this situation was observed in both age groups. Another limitation to the study is that six of the patients over 70 years of age did not have access to chemoradiotherapy in our hospital. These patients were classified as receiving standard treatment because there had been no discussion about treatment choice. Because elderly patients are often excluded from clinical trials, little information is available about toxicity after chemoradiotherapy in the elderly.

Finally, a multiple logistic regression analysis showed that age itself influences treatment choice even when correcting for comorbidity and other factors. This means that age is not merely a marker for other factors that determine treatment choice. Within the elderly age group, the factors of tumour stage and site, marital state, comorbidity, pain, physical functioning, appraisal support and opinions about the length of life are all determinants for non-standard treatment. Some of these factors, such as the general health status of the patient, have evident clinical significance and should be considered in decisions about cancer treatment. Treatment choice also has to be based on the wishes and motivation of the patient. However, we have to be alert to the fact that older patients might reject standard treatment because of misinformation and lack of social support. This misinformation might be aggravated by the surgeons' misconception of elderly patients' resilience. We must realise that ageing is a highly individualised process. A patient's chronological age does not necessarily reflect his or her biological or physical age. The treatment choice should be based on a medical assessment and the preferences of the patient, not on chronological age.

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