



Health-related quality of life after oral cancer treatment: 10-year outcomes

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Objective. The aim of this study was to report 10-year health-related quality of life (HRQOL) outcomes after treatment of oral squamous cell carcinoma (OSCC).

Study Design. Cross-sectional HRQOL surveys collated over a 13-year period for patients treated from 1992 yielded a cohort of 674 patients with OSCC who had undergone treatment with curative intent. HRQOL closest to 2 and 10 years was measured by using the University of Washington Quality of Life (UW-QOL) questionnaire.

Results. UW-QOL data were available for 67% (154) of 230 patients alive at 10 years. Three-quarters reported their overall quality of life (QOL) as good, very good, or outstanding. Free-flap surgery was the strongest predictor of overall QOL being less than good at 10 years. A significant problem or dysfunction, ranging from 7% to 13% across the 12 UW-QOL domains, was reported by a minority of patients. At the group level, the changes from 2 years to 10 years were minimal, with some improvement observed in appearance, chewing, mood and anxiety, and deterioration in swallowing. There was considerable scatter in individual changes over time.

Conclusions. At the group level, HRQOL at 10 years was similar to that at 2 years; however, at the individual-patient level, the domains were not so stable. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;130:144–149)

Health-related quality of life (HRQOL) is a key outcome of treatment for head and neck cancer (HNC).¹ Although there are numerous publications in this field,² there are only a few articles reporting on long-term HRQOL outcomes in HNC^{3–9} and even fewer reporting specifically on oral cancer.^{10,11} The earlier literature has tended to consider “long term” in terms of several previous years after diagnosis and treatment; however, “late effects” has emerged as an important issue, so outcomes should be considered beyond 5 years. The importance of long-term outcomes and survivorship is reflected in national documents and initiatives for all cancers. Also, now there is better appreciation of late effects and how these might have an impact on HRQOL.¹²

Bjordal et al.^{3,4} reported high levels of disease- and treatment-related symptoms, such as dryness in the mouth, mucus production, and psychological distress (30% of “cases” according to the General Health Questionnaire-20 [GHQ-20]), 7 to 11 years after radiotherapy for HNC. We have previously reported quality of life (QOL) 5 to 10 years after primary surgery for oral and oropharyngeal cancers; however, this was a small (48 patients) cross-sectional study.⁵ The findings of that study suggested that long-term survivors tend to

report good or excellent QOL, with outcomes similar to those at 1 year. This result is at variance with Mehanna et al.,⁷ whose cohort showed deterioration in overall QOL (life satisfaction) after 10 years, although those authors also had a small sample size and a cross-sectional design. Yan and coworkers¹¹ reported QOL 8 years after oral cancer, in a prospective study with 30 long-term survivors. Clinically and statistically significant improvements between diagnosis and 8 years were seen with regard to pain, mood, and anxiety, whereas problems with chewing, speech, shoulder mobility, and taste worsened.

The findings from the small number of studies so far are inconclusive, and the aims of this study was to report the HRQOL outcomes at around 10 years and compare them with those reported at 2 years in a larger number of patients with oral cancer.

MATERIAL AND METHODS

Patients

The population comprised all patients presenting with oral squamous cell carcinoma (OSCC) at the Aintree University Hospital between January 1, 1992, and August 31, 2004. Patients treated with palliative intent, those with cognitive impairment, and those living overseas were excluded.

Statement of Clinical Relevance

With regard to long-term health-related quality of life after oral cancer, 10-year outcomes are very important when reporting the results of treatment. This is the first study to report large numbers and to be able to look specifically at difference between 2 years and 10 years.

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Received for publication Dec 8, 2019; returned for revision Feb 16, 2020; accepted for publication Feb 25, 2020.

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2212-4403/\$-see front matter

<https://doi.org/10.1016/j.oooo.2020.02.018>

Variables and measurements

The University of Washington Quality of Life (UW-QOL) questionnaire is a well-established one,² and from 1995, we have regularly used this to survey patients with OSCC at various stages after primary diagnosis. The UW-QOL version 4 questionnaire consists of 12 single-item domains, with 3 to 5 response options scaled evenly from 0 (worst) to 100 (best) according to response hierarchy.¹³ UW-QOL domains are presented within 2 subscales: physical function and social–emotional function, as derived from an earlier work.¹⁴ The physical function domain score is the mean of the appearance, swallowing, chewing, speech, taste, and saliva domain scores, whereas the social–emotional function score is the mean of the pain, activity, recreation, shoulder, and mood and anxiety domain scores. We computed the subscale scores if 4 or more domain scores were available, and published criteria were used to identify which patients had a significant problem or dysfunction.¹⁵ There is also a single-item overall QOL question on the UW-QOL version 4 questionnaire, for which patients are asked to consider not only physical and mental health but also other factors, such as family, friends, spirituality, and personal leisure activities important to their enjoyment of life.

For patients alive at 10 years, their UW-QOL record closest to 10 years was selected within a time window requirement, that is, at least 8 years on from the baseline (primary surgery or diagnosis if no surgery). All of these records were made after year 2000, and hence UW-QOL version 4 was used. To enable comparison of UW-QOL close to 2 and 10 years for patients alive at 10 years, their UW-QOL record closest to 2 years was selected within a time window of 12 to 36 months. Many patients with records close to approximately 2 years responded to earlier versions of the UW-QOL, in which the taste, saliva, mood, and anxiety domains, in particular, were absent.

Statistical analysis

Fisher's exact test was used to test for the association between baseline categories with survival at 10 years and overall QOL being less than good after 10 years. Responses to each UW-QOL domain were summarized into 3 categories: dysfunction, best possible response, and responses that fell between these 2 extremes. With regard to within-patient change data over time (2 and 10 years), McNemar's test (2 categories) or the McNemar-Bowker test (3 categories) was used to test paired table symmetry. Cohen's kappa coefficient was used to measure agreement in paired categorical data over time; values less than 0.20 reflect "poor" agreement; 0.21 to 0.40 "fair"; 0.41 to 0.60 "moderate"; 0.61 to 0.80 "good"; and greater than 0.80 "very good." The paired *t* test was used to compare paired numerical UW-QOL domain

scores over time, and 95% confidence intervals (CIs) for the mean change were computed. Wilcoxon's test was used to compare paired subscale scores.

This study was approved by the Aintree University Hospital Audit Department as part of annual surveys and data collected in routine care.

RESULTS

Table I shows the 674 eligible patients and their characteristics. Overall survival at 10 years was 34% (230 of 674; 95% CI 30.5%–37.8%). Baseline age, tumor staging, free-flap surgery, and primary treatment were associated ($P < .001$) with overall survival at 10 years (see Table I). UW-QOL data closest to 10 years (and at least 8 years on) was available for 67% (154 of 230), at a median (interquartile range [IQR]) of 121 months (range 117–125 months) from baseline. Free-flap surgery was the strongest predictor of overall QOL being less than good at 10 years (see Table I): 45% for patients with composite flaps, 26% for those with soft flaps, and 14% for those without free flaps. Other negative prognostic trends were observed for advanced tumors and for patients earlier in the cohort, although it was noted that the use of composite flaps fell from 25% in 1992–1996 to 12% in 2002–2004 and the use of any free flap from 81% to 64%.

A significant problem or dysfunction was indicated from the responses given by a minority of patients, ranging from 7% to 13% across the 12 UW-QOL domains (Table II). Otherwise, there was a fairly even split in patient response between the best possible response (35%–50% across domains) and being somewhere between the 2 extremes (33%–54%). Overall QOL was good or better for 74% (112 of 151) and subscale median scores of the median physical function and of the social–emotional function were 80 and 83, respectively (Table III).

Tables IV and V show the UW-QOL domain results for 113 patients with data close to 10 years (at least 8 years on) at a median (IQR) of 121 months (range 117–124 months) and close to 2 years (within 12–36¹ months) at a median (IQR) of 25 months (range 20–28 months). The main observation was that changes in the UW-QOL results were quite similar at 2 and 10 years with regard to the domain categorizations (see Table IV) and numerical mean domain scores (see Table V). Both tables indicate small improvements in appearance, chewing, mood, and anxiety and deterioration in swallowing. Within-patient Kappa agreement between categories at 2 and 10 years was generally fair to moderate, with slightly more agreement observed for the physical function domains than for

¹ Lines 204/205 of results. Their editing hasn't worked here, hence need to replace "...and subscale median scores of the median physical function and of the social-emotional function" with "...and subscale median scores of physical function and of social-emotional function"

Table I. Baseline characteristics and overall quality of life (QOL) for those alive at 10 years

Baseline characteristics		Alive at 10 years		P value*	Overall QOL less than good [†]		P value*	Median No. of months to UW-QOL questionnaire
		%	n/N		%	n/N		
Year	TOTAL	34	230/674		26	39/151		121
	1992–1996	36	83/232	.53	34	20/58	.08	123
	1997–2001	35	94/269		24	16/67		121
	2002–2004	31	53/173		12	3/26		115
Gender	Male	32	137/426	.18	25	24/95	.84	121
	Female	38	93/248		27	15/56		122
Age (years)	< 55	50	86/172	< .001	32	19/60	.39	123
	55–64	40	79/196		21	12/58		121
	65–74	28	47/169		24	8/33		119
	75+	13	18/137					
Tumor site	Buccal	28	38/134	.02	37	10/27	.08	123
	Lower gum	32	24/76		25	3/12		120
	Tongue (anterior two-thirds)	44	87/200		20	11/56		120
	Floor of mouth	32	69/215		20	9/45		121
	Other	24	12/49		55	6/11		123
Overall clinical stage	Early (0–2)	45	150/332	< .001 excl. NK	22	22/102	.11	121
	Late (3–4)	24	80/339		35	17/49		121
	NK		0/3					
Primary treatment	Surgery alone	45	166/367	< .001	25	27/107	.83	122
	Surgery and RT	24	59/241		29	12/42		121
	Radiotherapy alone	8	5/66		0	0/2		108
Free flap surgery	Yes—composite	27	45/169	.001	45	13/29	.01	123
	Yes—soft	38	103/271		26	20/77		122
	No flap	46	77/168		14	6/43		119
Pathological stage (surgical cases)	Early (0–2)	51	131/258	< .001 excl. NK	20	18/88	.06 excl. NK	122
	Late (3–4)	28	93/333		34	21/61	NK	121
	NK	6	1/17		0	0/2		105

NK, not known; QOL, quality of life; UW-QOL, University of Washington Quality of Life questionnaire.

*Fisher’s exact test.

[†]151 of 230 alive at 10 years had overall QOL recorded from at least 8 years (96 months) on.

the social–emotional function domains (see Table IV).² The standard deviations (SDs) for individual change scores indicate considerable scatter between 2-year and 10-year scores (see Table V).

With regard to overall QOL being less than good, the agreement between the 2- and 10-year scores was weak (kappa statistic of 0.21) and the increase observed overall (from 14% [10 of 73] to 19% [14 of 73]) was not statistically significant (McNemar’s test; $P = .45$). Median (IQR) physical function subscale scores were 74 (range 66–91) at 2 years and 78 (range 64–91) at 10 years ($P = .50$; Wilcoxon’s paired test; $n = 112$); median (IQR) social–emotional function subscale scores were 83 (range 69–92) at 2 years and 83 (range 70–95) at 10 years ($P = .39$; Wilcoxon’s paired test; $n = 113$).

DISCUSSION

There is a paucity of HRQOL data collected prospectively to 10 years after oral cancer. This is an important topic in respect to survivorship and late effects. Although our unit has published outcomes research on both HRQOL¹⁶ and survival after oral cancer,¹⁷ longitudinal changes up to 10 years have not been reported before. Our longitudinal design allows comment on changes from 2 years to 10 years, and this study has the strength of being a relatively large sample of responders (154 patients) with 10-year HRQOL data and an acceptable response rate (67%). The study has some limitations. First, the responses to the UW-QOL questionnaire was not collected at fixed time points during follow-up but as part of “annual” surveys, and hence the use of time windows to capture data close to certain time points. Second, with the aging patient population in the study, no attempt was made to account for other comorbidities, which might impact negatively on HRQOL. The sample is one of survivorship, with patients dropping out probably reporting worse HRQOL. Third, the cohort was inevitably historical

²Table 4, last row of results, the change P value. Given the way they have edited other P values then the value “0.27” should be “.27

Table II. UW-QOL domain results for 154 OSCC patients alive at 10 years

		No.	Mean (SE) score	Dysfunction		Somewhere between		Best response	
UW-QOL—Physical function subscale	Appearance	153	78.6 (1.6)	10%	16	53%	81	37%	56
	Swallowing	153	79.9 (2.2)	12%	19	34%	52	54%	82
	Chewing	151	71.9 (2.5)	7%	10	43%	65	50%	76
	Speech	153	81.1 (1.7)	7%	10	47%	72	46%	71
	Taste	152	74.6 (2.5)	9%	13	43%	65	49%	74
	Saliva	150	76.0 (2.3)	10%	15	44%	66	46%	69
UW-QOL—Social—emotional function subscale	Pain	153	83.0 (1.8)	9%	14	37%	56	54%	83
	Activity	153	73.4 (2.0)	12%	19	50%	77	37%	57
	Recreation	153	77.6 (1.8)	7%	11	54%	82	39%	60
	Shoulder	152	78.1 (2.4)	13%	19	33%	50	55%	83
	Mood	154	80.5 (2.0)	12%	18	39%	60	49%	76
	Anxiety	152	82.0 (1.8)	9%	13	39%	59	53%	80

Of the 230 alive at 10 years, 154 had UW-QOL data recorded from at least 8 years (96 months) on. SE, standard error; UW-QOL, University of Washington Quality of Life questionnaire.

Table III. UW-QOL subscale scores and overall QOL at 10 years for patients with OSCC

Physical function subscale score (0–100):		
<50	12%	19/153
50–69	21%	32/153
70–89	30%	46/153
90–100	37%	56/153
Median (IQR) score	80 (65–95), N = 153	
Social-emotional function subscale score (0–100):		
<50	9%	14/154
50–69	16%	24/154
70–89	40%	61/154
90–100	36%	55/154
Median (IQR) score	83 (70–95), N = 153	
Overall QOL:		
Very poor/Poor	7%	10/151
Fair	19%	29/151
Good	36%	54/151
Very good/Outstanding	38%	58/151
Good or better	74%	112/151

Of the 230 alive at 10 years, 154 had UW-QOL data recorded from at least 8 years (96 months) on.

Subscale scores were computed if 4 or more domain scores were available.

IQR, interquartile range; OSCC, oral squamous cell carcinoma; QOL, quality of life; UW-QOL, University of Washington Quality of Life questionnaire.

(1992–2004), and various new treatment strategies have since emerged, such as intensity-modulated radiation therapy (IMRT), which could influence the long-term outcomes in the more recently treated patients.

Our sample does reflect survivorship in so much as there are relatively few patients 65 years of age or older at the time of treatment and who are alive after 10 years and contributing UW-QOL outcomes data, especially those age 75 years and greater. Similarly, those with advanced stages of disease, those who have had surgery and postoperative radiotherapy, and those requiring composite free tissue transfer are relatively fewer at longer-term follow-up than during treatment. This

might partly explain the relatively good survival rate and relatively consistent reported QOL characteristics between 2 and 10 years.

The long-term HRQOL outcomes that we have reported here appear to be relatively good across the UW-QOL domains with regard to dysfunction and high mean scores. Three-quarters of the patients stated that their overall QOL was good or better. Some domain scores, such as activity, chewing, taste and saliva, could be expected to fall naturally with age, but we could not explore this further as because normative data for the UW-QOL domains over time does not exist.¹⁴

It is very difficult to directly compare the findings of this present study with those of previous studies because of the different case mix characteristics. Yan et al.¹¹ reported change in UW-QOL scores from 1 year to 8 years in 30 oral cancer survivors. In this period, patients reported clinically significant improvements in appearance, recreation, speech, saliva, and anxiety, whereas the scores of the other 7 items remained stable. In a cross-sectional survey using the UW-QOL questionnaire, of the 26 patients, median age 14.7 years (range 3–27 years) after treatment for oral cancer when they were 40 years of age or less, 77% rated their overall QOL as outstanding, very good, or good.¹⁰ Only radiotherapy seemed to adversely affect the overall QOL, and the key domains affected were appearance, mood, saliva, and shoulder function. Long-term outcomes with good to very good QOL were reported by 67 patients, 2 to 10 years after preoperative chemoradiotherapy followed by surgery, including microvascular reconstruction for advanced oral and oropharyngeal cancers.⁶ In contrast, a longitudinal assessment of 26 patients treated for advanced oral or oropharyngeal cancer, with a mean follow-up of 9.2 years (range 8–11 years), reported that a number of HRQOL domains worsened significantly ($P < .01$) in the long term: emotional functioning, social functioning, swallowing, speech, taste/smell, dry mouth, sticky saliva, and

Table IV. UW-QOL dysfunction at 2 and 10 years

	No. at 2 and 10 years		2 years		10 years		Change P value*	Kappa coefficient of agreement (SE) between the 3 categories over time			
	Dysfunction	Somewhere between	Best response	Dysfunction	Somewhere between	Best response					
									Dysfunction	Somewhere between	Best response
UW-QOL—Physical function subscale	101	60%	61	30%	30	8%	8	54%	38	.08	0.32 (0.08)
Appearance	112	5%	44	55%	62	13%	15	33%	60	.03	0.43 (0.07)
Swallowing	111	6%	61	39%	43	5%	6	47%	53	.12	0.42 (0.08)
Cheewing	112	3%	68	37%	41	6%	7	52%	47	.18	0.55 (0.07)
Speech	77	9%	28	55%	42	6%	5	43%	39	.38	0.54 (0.09)
Taste	73	14%	30	45%	33	11%	8	44%	33	.21	0.59 (0.08)
Saliva	107	8%	35	59%	63	8%	9	34%	62	> .99	0.50 (0.08)
Pain	100	4%	52	44%	44	9%	9	48%	43	.19	0.19 (0.09)
Activity	107	8%	54	41%	44	5%	5	52%	46	.62	0.43 (0.08)
Recreation	107	11%	24	66%	71	10%	11	31%	63	.50	0.22 (0.08)
Shoulder	74	11%	33	45%	33	4%	3	42%	40	.02	0.36 (0.09)
Mood	73	12%	29	48%	35	5%	4	40%	40	0.27	0.35 (0.09)
Anxiety											

SE, standard error; UW-QOL, University of Washington Quality of Life questionnaire.

*McNemar-Bowker test.

coughing.⁸ However, this was a group of patients who had been treated with free flap reconstruction and postoperative radiotherapy, and this could account for the deterioration. In an assessment of 22 patients at 10 years after organ preservation treatment, long-term functional voice and speech problems were common, with fewer complaints in those treated with IMRT than in those treated with conventional radiotherapy,¹⁸ as well as difficulty swallowing and reduced mouth opening.¹⁹

When comparing overall HRQOL at 2 years and at 10 years in our sample, it was notable that in this cohort of patients, there was relatively little change at the group level. At most, the mean changes were in the order of 4 to 6 units. According to Kazis et al.²⁰ effect size can be obtained by dividing mean change by the SD in prechange data, and a “small” effect represents about 0.20 of SD, a “moderate” effect about 0.50 of SD, and a “large” effect about 0.80 of SD. Our results at 1 to 2 years gave domain SDs of around 20, and this indicates a “small” mean change being equivalent to 4 units, a “moderate” change being equivalent to 10 units, and a “large” change being equivalent to 16 units. Ringash et al.²¹ defined “minimal important difference” as the smallest difference that reflects a clinically important change in scores and stated that most published minimal important difference estimates fell into the range of 5% to 10% of the instrument range, which, for us, implied mean changes of about 5 to 10 units. Thus, it is reasonable to suggest that the changes between mean scores at 2 and 10 years we observed were small and just bordering on being clinically significant. There were improvements in appearance, chewing, mood, and anxiety and deterioration in swallowing. Although, in the whole cohort, HRQOL appeared relatively stable after 2 years, there were individual variations. Our data show considerable individual scatter in domain change scores (see Table V) and only fair to moderate agreement between 2 and 10 years with regard to the 3 categories (see Table IV, “dysfunction,” “neither extreme,” “best possible”). It is hard to ignore that in Table IV, there was no Cohen’s kappa score greater than 0.60, which is the generally held criterion for defining good agreement, and thus, there was considerable within-patient instability between the results seen at 2 years and at 10 years.

CONCLUSIONS

In the long term, after oral cancer treatment, most patients report good or better overall QOL. Those alive at 10 years were considered survivors, with survival linked to the baseline characteristics, because those older and with advanced cancer were lost to follow-up. Group level changes between 2 and 10 years were small, with some bordering on being clinically significant, with improvements in appearance, chewing, mood, and anxiety and deterioration in swallowing. Changes at the individual-patient level were not so stable.

Table V. UW-QOL mean domain scores at 2 and 10 years

		No. at 2 and 10 years	2 years Mean (SE)	10 years Mean (SE)	Change Mean (SD)	95% CI: mean change	P value*
UW-QOL—Physical function subscale	Appearance	112	74.3 (1.9)	78.8 (1.8)	4.5 (21.5)	0.4, 8.5	.03
	Swallowing	112	84.2 (1.9)	79.9 (2.5)	-4.3 (25.0)	-9.0, 0.4	.07
	Chewing	111	66.2 (2.8)	71.2 (2.8)	5.0 (29.3)	-0.6, 10.5	.08
	Speech	112	79.9 (1.6)	80.1 (1.8)	0.2 (17.3)	-3.1, 3.4	.91
	Taste	77	80.4 (3.0)	76.9 (3.3)	-3.5 (22.7)	-8.7, 1.6	.18
UW-QOL—Social—emotional subscale	Saliva	74	74.2 (3.4)	74.3 (3.5)	0.1 (24.6)	-5.6, 5.8	.96
	Pain	113	83.2 (2.1)	82.5 (2.2)	-0.7 (18.8)	-4.2, 2.8	.71
	Activity	112	77.5 (2.1)	75.5 (2.3)	-2.0 (24.7)	-6.6, 2.6	.39
	Recreation	113	78.5 (2.1)	79.6 (2.0)	1.1 (21.2)	-2.9, 5.1	.58
	Shoulder	110	81.3 (2.9)	80.5 (2.6)	-0.8 (27.8)	-6.1, 4.4	.76
	Mood	74	79.0 (2.9)	85.1 (2.3)	6.1 (25.8)	0.1, 12.1	.05
	Anxiety	74	79.0 (2.9)	84.2 (2.3)	5.2 (24.6)	-0.5, 10.9	.08

CI, confidence interval; SD, standard deviation; SE, standard error; UW-QOL, University of Washington Quality of Life questionnaire. *Paired t test.

ACKNOWLEDGMENTS

We thank the patients for contributing to this investigation through their completion of “annual” surveys.

DISCLOSURE

Although the study had no formal financial support, D.L. was funded by charitable donations to the HaNC (<http://www.hancsupport.com/event/patient-research-forum>).

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