

Health-related quality of life in T1N0 oral squamous cell Carcinoma: Selective neck dissection compared to wait and watch.

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Keywords

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Abstract

There are controversies in the management of the neck in clinical T1N0 oral squamous cell carcinoma (OSCC). The aim of this study was to describe a consecutive cohort of stage 1 OSCC patients and report their HRQOL at a time closest to two years after primary surgery. Of 216 patients treated between 2007-2012, 195 were eligible for the analysis of health related quality of life (HRQoL), after excluding early death and regional recurrence. This was measured using the University of Washington Quality of Life V4 questionnaire.

Overall response was 65% (126/195). The HRQoL outcomes were good. However, there were more clinically significant problems for patients in the SND group than W&W in appearance (14% Vs 1%, $P=0.008$) and pain (19% Vs 6%, $P=0.04$). Similar trends were seen for shoulder (14% Vs 8%), mood (16% Vs 8%) and speech (5% Vs 1%) and for overall quality of life being less than good (30% Vs 16%).

It is difficult to tease out why patients did or did not have neck dissection in a retrospective sample, but it is likely that those with SND could have had larger stage 1 tumours. The findings highlight the importance of SND on HRQOL in domains such as appearance, pain, speech, swallowing and chewing. Previous studies in SND have tended to focus on accessory nerve injury and shoulder function, however this new data emphasises the need to include other domains in future trials comparing W&W, SND and sentinel lymph node biopsy.

Introduction

It has been appreciated for many years that neck dissection causes morbidity that impacts on health related quality of life (HRQoL).¹ Management of the neck in T1/T2 N0 oral squamous cell carcinoma (SCC) is controversial. Treatment options include wait and watch (W&W), sentinel lymph node biopsy (SLNB),² and selective neck dissection (SND).³ Recent guidelines recommend surgical management of the neck as an option in early stage oral SCC.⁴

Both optimal survival and HRQoL are important considerations.⁵ Neck dissection has been shown to improve survival in patients with early oral cancer.⁶ Patient reported outcomes following neck dissection have shown lower HRQoL in those undergoing neck dissection than those with no neck dissection⁷. Incrementally poorer quality of life is seen with selective neck dissection (SND), modified radical neck dissection (MRND) and radical neck dissection (RND).⁷ There is some evidence that shoulder morbidity is increased when level 2b is included in the neck dissection.^{8,9}

Patients undergoing W&W management of the neck have better HRQoL than those undergoing neck dissection.⁷ This needs to be balanced against the risk of neck failure, the need for further treatment, and disease specific survival. It is likely that tumours with minimal depth of invasion have a low risk for cervical metastasis, hence might be more suitable for a W&W approach,¹⁰ however even relatively superficial lesions can metastasise. A prospective randomised controlled trial suggested that there may not be a survival advantage with surgical treatment of the clinically node negative neck in tumours less than 3mm thick.⁶ It is currently not possible to stratify patients into a low risk group based on tumour thickness or by any other means. The decision on the optimal managing for the N0 neck and balance of risks will be different for each patient. Better understanding of morbidity can help inform patients to make this decision for themselves.

Others have shown SLNB has no survival disadvantage in the T1 and T2 N0 OSCC group compared to SND.^{2,11} There is some evidence to suggest SLNB in this setting may be associated with better functional outcomes and HRQoL than SND but evidence is weak.^{12,13} It is possible that SLNB maintains the survival advantage of SND but retaining the HRQoL advantages of W&W. Neither assumption is yet certain.

The main determinants of HRQoL in larger (T3/T4) oral SCC are the use of free flaps and post-operative radiotherapy.⁵ The impact of a neck dissection and shoulder dysfunction is less of a HRQoL issue than dry mouth, speech, saliva or chewing.¹⁴ In contrast, patients with T1 and T2 OSCC seem to incur more morbidity from neck dissection than from surgery to the primary site. There are very few papers that have sufficient patients with stage 1 oral cancer to allow adequate comparison between wait and watch and SND.¹³ Hence, the aim of this study was to describe a consecutive cohort and report their HRQoL at a time closest to two years after primary surgery.

Methods

Audit approval was obtained from the Aintree University Hospital Audit Department and patients were identified using the Aintree head and neck oncology database. Consecutive patients with clinical T1 N0 OSCC treated by primary surgery with curative intent between January 2007 and December 2012 were included. The study period was immediately before the introduction of SLNB to the unit. SLNB was therefore not an option for these patients. Operative and pathology records were reviewed. Follow-up information to February 2016 was obtained from clinical notes and letters. Patients with disease beyond clinical stage I and those treated with palliative intent were excluded. It is the practice of the unit to send the University of Washington Quality of Life (UW-QOL) questionnaire to patients following treatment. The UW-QOL questionnaire completed at a time-point closest to 24 months and a minimum of 9 months from operation, was analysed.

The UW-QOL questionnaire is well established.¹⁵ Version 4 consists of 12 single question domains, each having between 3 and 6 response options scaled evenly from 0 (worst) to 100 (best) according to response hierarchy. For this study, we used criteria derived from earlier work to determine the domains in which patients had a 'significant problem/dysfunction'.¹⁶ These criteria are based on a mix of domain scores and the importance of domains during the previous week. We also analysed the UWQOL using its two subscale composite scores 'Physical function' and 'Social-emotional function' and a single six-point 'overall' QOL measure.¹⁷ Physical function is the simple average of the swallowing, chewing, speech, saliva, taste and appearance domain scores whilst social-emotional function is the simple average of the activity, recreation, pain, mood, anxiety and shoulder domain scores. Finally, a single item overall QOL scale was used. Patients were asked to consider not only physical & mental health, but also other factors, such as family, friends, spirituality or personal leisure activities important to their enjoyment of life.

The aim was to describe HRQoL approximately two years after surgery in patients who had a neck dissection and those under wait and watch surveillance without regional recurrence. Comparative tests were performed in availability of UWQOL data by baseline characteristics, between neck dissection and wait and watch groups in baseline characteristics and in UW-QOL responses. The Mann-Whitney test was used to compare groups for age and UWQOL subscale scores. Statistical significance was set at the 5% level.

Results

Two hundred and sixteen patients met the inclusion criteria, 168 wait and watch and 48 with neck dissection. Twenty-one of these were excluded from analysis of QOL data: regional recurrence (12 wait and watch, 1 neck dissection), death within 9 months (7 wait and watch), and one wait and watch patient who presented with a synchronous laryngeal tumour treated by RT. This left 47 who had a neck dissection and 148 who had wait and watch surveillance. UW-QOL data at least 9 months after operation were available for analysis in 79% (n=37/47) of the neck dissection group (median 24 months, IQR 21-29 months after surgery) and in 60% (n=89/148) of the wait and watch group (median 22 months, IQR 19-27 months). There was a higher rate of UW-QOL data being available (80% 68/85 Vs 53% 58/110) for the earlier

2007-9 cohort than for the 2010-12 cohort and also (79% 37/47 Vs 60% 89/148) for the neck dissection group . Otherwise there was no notable variation by gender, age group, site or primary tumour or treatment (results not shown). Neck dissection patients with UWQOL data were 6 years younger on average than wait and watch patients (Table 1) and more had tumours located in the anterior two-thirds of the tongue (73% Vs 53%). The neck dissection group was also characterised by 11 (30%) having surgery involving free-flap tissue transfer and 3 (8%) being treated with adjuvant radiotherapy.

Quality of life after about two years was worse for patients having a neck dissection than for patients in the wait and watch group (Table 2). This was seen for both physical ($P<0.001$) and social-emotional ($P=0.04$) functioning and for overall QOL being rated as less than good (30% Vs 16%, $P=0.09$). More clinically significant dysfunction was seen in patients in the neck dissection cohort (Table 3) for appearance (14% Vs 1%, $P=0.008$) and pain (19% Vs 6%, $P=0.04$). Similar trends were seen in the shoulder (14% Vs 8% $P=0.34$), mood (16% Vs 8% $P=0.21$) and speech (5% Vs 1% $P=0.21$) domains. When results were grouped into those with the best possible domain responses and those with lesser scores (Table 3), patients in the neck dissection cohort reported lower levels of HRQOL in all domains except anxiety. The most notable differences were in regard to appearance ($P<0.001$), speech ($P<0.001$), swallowing ($P=0.008$), chewing ($P=0.02$) and pain ($P=0.02$).

When patients having had either free tissue transfer or radiotherapy were excluded (all from the neck dissection group), similar findings were obtained. Overall quality of life was worse with neck dissection (29%, 7/24) compared with watch and wait (16%, 14/87 as per Table 2), $P=0.15$. Physical function ($P<0.001$) and social-emotional ($P=0.14$) scores were also worse in neck dissection patients, with median (IQR) scores of 84 (69-95) and 83 (63-98) respectively. More clinically significant dysfunction was seen in neck dissection patients (Table 3) for appearance ($P=0.03$), with similar trends for pain (13% Vs 6%), shoulder (13% Vs 8%), mood (13% Vs 8%) and speech (4% Vs 1%) domains. With regard to achieving best possible domain responses neck dissection patients reported lower levels of HRQOL in all domains except anxiety and saliva (Table 3).

Discussion

Relatively few studies report HRQOL outcomes for early stage oral cancer.^{12,18} There is a growing recognition of the importance of HRQoL in the decision making process and resources are available to aid clinicians in this regard.²⁵ The aim of this study was to describe HRQOL outcomes of patients having undergone SND or W&W in T1N0 oral SCC. The sample size is adequate and the questionnaire response rate is comparable to other HRQOL studies.^{13,18} The SND cohort was smaller which reflects that W&W strategy was routinely offered for smaller tumours at the time of data collection. From a retrospective sample it is difficult to understand why patients did or did not have neck dissection. This limitation is acknowledged. It is likely those

having SND had larger stage 1 tumours. Another issue is that this study reports survivors who have not had neck failure. Of the 13 with neck failure, only 4 had HRQoL data, so this small subgroup were excluded from the analysis..

Appearance change after neck dissection is multifactorial. While 83% of the wait and watch group rated themselves with the best possible response, only 22% of those with a neck dissection did so ($P<0.001$). Weakness of the marginal mandibular branch of facial nerve causing smile asymmetry, cervical scar, tissue hollowing, radiotherapy, fibrosis and loss of skin mobility can all contribute. Weakness of the marginal mandibular branch of the facial nerve has been reported as being present in 18% of neck dissections but, severe injuries were rare (3%).¹⁹ Scarring after neck dissection may affect HRQoL. One study showed that SLNB resulted in a smaller scar, better skin complexion and less soft tissue deficit than END.¹² All types of neck dissection appear to cause fibrosis causing stiffness, constriction and appearance change and low HRQoL scores in these domains.²⁰ In one study neck tightness was severe enough to cause interference with daily activities in 37%, but reduced over time.²¹ There is currently no data on these issues after SLNB.

Pain and numbness are common complaints after neck dissection. In our study 19% of END patients and 6% of the W&W group reported significant dysfunction ($P=0.04$). Another large study found 34% of patients had neck pain after SND versus 12% after surgical treatment of the primary cancer without neck dissection.⁷ Preservation of the cervical root branches has also been shown to decrease pain and improve HRQoL.^{22,23}

The severity of shoulder symptoms has been shown to relate to the type of surgery performed.^{9,13} Our data suggests worse HRQoL with SND than W&W, though differences were statistically non-significant. Sacrificing the spinal accessory and cervical nerves results in more morbidity than when these nerves are spared.^{9,23} SLNB has been shown to give better shoulder function than SND but worse functional outcomes than W&W.¹³ SLNB will likely avoid dissection of the spinal accessory and cervical nerves and its associated morbidity in most patients. Further research is required to assess if this translates into a clinically meaningful improvement in HRQoL. Despite there being measurable differences in shoulder outcomes between accessory nerve sparing neck dissections and the non-operated population, HRQoL outcomes in the surgical cohort still tend to be good.⁵

Speech was reported as a clinically significant problem in 5% of the SND group cohort and 1% of the W&W cohort. Eighty percent of the W&W group and 41% of the END group gave the best possible response regarding speech ($P<0.001$). Another study found that 24% of SND and 11% of W&W patients reported impaired speech 6 months after surgery.⁷ It is unclear in our study if the difference in speech is related to differences in tumour resection in the two groups.

In this study, neck dissection patients were around 6 years younger on average and had more tumours located in the anterior two-thirds of the tongue. These characteristics could account for some of the differences in HRQoL between the

groups, as could other factors not measured in this study such as depth of invasion. After exclusion of patients who had free tissue transfer or radiotherapy (all from the ND group), similar findings were obtained. The intention was not to adjust for baseline characteristics but to accept the clinical differences inherent within the groups and to describe the HRQoL outcomes that clinicians might expect their patients to report. Another limitation of our study is that our findings are from a single unit and decision between W&W or SND in stage 1 oral cancer might vary in other cancer centres.

Since our data collection, evidence and guidelines have changed. SLNB is now an option for surgical staging. While this is a smaller undertaking than neck dissection, the evidence of patient reported outcome measures are yet to be determined,^{13,24} and is subject to ongoing research. Many healthcare economies will not have the infrastructure to provide SLNB, hence the comparison to W&W is valid. More data is needed to adequately inform patient decision making. Our study indicates that for stage 1 oral cancer we should move away from the traditional focus on accessory nerve injury and shoulder function and also report other aspects of HRQoL that are perhaps more important to patients such as appearance, pain, speech, swallowing and chewing. These domains should be included in future trials comparing outcomes between W&W, SND and SLNB.

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Table 1. Baseline clinical and demographic characteristics of 37 patients who had neck dissection and of 89 who were under wait and watch surveillance. All were without regional recurrence and had UW-QOL data available for analysis.

		% with QOL Neck dissection N=37	% with QOL Wait and watch N=89	P Value*
Gender	Male	54% (20)	58% (52)	0.70
Age	<55 years	35% (13)	22% (20)	0.33
	55-64 years	32% (12)	35% (31)	
	≥65 years	32% (12)	43% (38)	
	Median (IQR) years	58 (52-66)	64 (55-69)	0.06
Site of primary tumour	%Tongue (ant 2/3)	73% (27)	53% (47)	0.09
	%Floor of mouth	14% (5)	30% (27)	
	%Other	14% (5)	17% (15)	
Year of treatment	2010-2012	35% (13)	51% (45)	0.12
Free-Flap (soft)	Yes	30% (11)	0% (0)	<0.001
Adjuvant Radiotherapy	Yes	8% (3)	0% (0)	0.02

*Fishers exact test, apart from Mann-Whitney test for age in years

Table 2. UW-QOL subscale scores and overall QOL results for 37 patients who had neck dissection without regional recurrence and 89 who were under wait and watch surveillance without regional recurrence.

	Neck dissection N=37	Wait and watch N=89**	P value*
Physical function subscale score (0-100): Median (IQR)	86 (70-95)	96 (87-100)	<0.001
Score <60	8% (3)	2% (2)	
60-69	16% (6)	3% (3)	
70-79	16% (6)	8% (7)	
80-89	19% (7)	15% (13)	
90-100	41% (15)	72% (63)	
Social-emotional function subscale score (0-100): Median (IQR)	83 (62-90)	91 (77-95)	0.04
Score <60	22% (8)	8% (7)	
60-69	8% (3)	11% (10)	
70-79	16% (6)	10% (9)	
80-89	27% (10)	18% (16)	
90-100	27% (10)	53% (47)	
% rating overall QOL as being less than good (i.e. as very poor, poor or fair)	30% (11/37)	16% (14/87)	0.09

*Mann-Whitney test for subscale scores and Fishers Exact test for overall QOL.

**Physical function subscale scores known for N=88

Table 3. UW-QOL domain results for patients who had neck dissection without regional recurrence and for those who were under wait and watch surveillance without regional recurrence

		N	Mean domain score	Significant problem/dysfunction	In-between	Best response (score=100)	P value**	P value***
UW-QOL physical function:								
Appearance	Wait and watch	89	93.8	1% (1)	16% (14)	83% (74)		
	Neck dissection	37	73.0	14% (5)	65% (24)	22% (8)	0.008	<0.001
	Neck dissection*	24	76.0	13% (3)	58% (14)	29% (7)	0.03	<0.001
Swallowing	Wait and watch	89	94.8	1% (1)	13% (12)	85% (76)		
	Neck dissection	37	86.8	3% (1)	35% (13)	62% (23)	0.50	0.008
	Neck dissection*	24	88.8	0% (0)	38% (9)	63% (15)	>0.99	0.02
Chewing	Wait and watch	87	86.8	3% (3)	20% (17)	77% (67)		
	Neck dissection	37	75.7	3% (1)	43% (16)	54% (20)	>0.99	0.02
	Neck dissection*	24	79.2	0% (0)	42% (10)	58% (14)	>0.99	0.08
Speech	Wait and watch	88	93.4	1% (1)	19% (17)	80% (70)		
	Neck dissection	37	80.0	5% (2)	54% (20)	41% (15)	0.21	<0.001
	Neck dissection*	24	75.8	4% (1)	71% (17)	25% (6)	0.38	<0.001
Taste	Wait and watch	88	89.9	2% (2)	23% (20)	75% (66)		
	Neck dissection	36	80.3	6% (2)	39% (14)	56% (20)	0.58	0.05
	Neck dissection*	23	83.5	4% (1)	39% (9)	57% (13)	0.51	0.12
Saliva	Wait and watch	88	90.7	4% (4)	20% (18)	75% (66)		
	Neck dissection	36	84.7	3% (1)	33% (12)	64% (23)	>0.99	0.27
	Neck dissection*	24	89.2	4% (1)	21% (5)	75% (18)	>0.99	>0.99
UW-QOL social-emotional function:								
Pain	Wait and watch	88	90.1	6% (5)	22% (19)	73% (64)		
	Neck dissection	37	79.1	19% (7)	30% (11)	51% (19)	0.04	0.02
	Neck dissection*	24	81.3	13% (3)	38% (9)	50% (12)	0.37	0.05
Activity	Wait and watch	88	83.2	8% (7)	33% (29)	59% (52)		
	Neck dissection	37	77.7	5% (2)	54% (20)	41% (15)	>0.99	0.07
	Neck dissection*	24	79.2	4% (1)	58% (14)	38% (9)	>0.99	0.07
Recreation	Wait and watch	88	83.8	8% (7)	39% (34)	53% (47)		
	Neck dissection	37	77.7	5% (2)	60% (22)	35% (13)	>0.99	0.08
	Neck dissection*	24	81.3	0% (0)	63% (15)	38% (9)	0.34	0.25
Shoulder	Wait and watch	85	87.6	8% (7)	16% (14)	75% (64)		
	Neck dissection	36	77.2	14% (5)	28% (10)	58% (21)	0.34	0.08
	Neck dissection*	24	80.8	13% (3)	25% (6)	63% (15)	0.69	0.20
Mood	Wait and watch	87	82.2	8% (7)	40% (35)	52% (45)		
	Neck dissection	37	71.6	16% (6)	51% (19)	32% (12)	0.21	0.05
	Neck dissection*	24	74.0	13% (3)	58% (14)	29% (7)	0.45	0.07
Anxiety	Wait and watch	88	76.5	10% (9)	51% (45)	39% (34)		
	Neck dissection	37	74.3	14% (5)	46% (17)	41% (15)	0.75	0.84
	Neck dissection*	24	80.4	8% (2)	42% (10)	50% (12)	>0.99	0.36

*Excluding patients having had free-flap surgery and/or radiotherapy treatment.

**Fishers exact test comparing % with significant problem/dysfunction between the Neck Dissection and Wait & Watch groups

***Fishers exact test comparing % with best possible response between the Neck Dissection and Wait & Watch groups