Early Quality of Life Outcomes In Head And Neck Cancer Survivors With EORTC QLQ-C30 And EORTC QLQ-HN35 In An Asian Tertiary Center

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Abstract

Background The objective of the study was to evaluate the quality of life (QOL) of head and neck cancer survivors after treatment and to identify patients' main concerns. The study also aims to establish pre-treatment reference values particularly for the Asian patient. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) and Head and Neck module (EORTC QLQ-HN35) were used for objective evaluation.

Methods Patients planned for elective surgery for head and neck cancers were enrolled in the study. The questionnaires were completed at pre-treatment and at 6 months after surgery. Results were compared with previously published reference values.

Results 140 patients completed both questionnaires. Locally advanced tumour and extent of surgery [tracheostomy ($p<0.01$), surgical flap ($p<0.01$)] were associated with lower global health scores. Adjuvant treatment was also a contributory factor ($p<0.01$). Dysphagia and social eating was a primary concern within our population.

Conclusion Treatment of head and neck cancers is safe but there is poor QOL in the early post-treatment period especially with eating. Previously published data suggests improvement after a year.

Background

Head and neck malignancies are cancers that can arise from the lip, oral cavity, pharynx, larynx, salivary glands or the facial sinuses. Due to the complexity in the anatomy and functions of the head and neck region, curative multimodality treatment can result in considerable long-lasting morbidity. Ideal treatment requires a fine balance between adequate disease clearance and the preservation of reasonable form and function. As a result, patients may sometimes be left with chronic dysfunction which can impact their physical, social and emotional functions as well as their overall quality of life (QOL).¹⁻³

The European Organisation for Research and Treatment of Cancer Quality of Life (EORTC) Group introduced a survey tool in 1994 as a means of measuring the QOL in cancer patients. Since then, there has been refinement of the questionnaires with specific disease site modules. The EORTC Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) and the EORTC Quality of Life Questionnaire-Head and Neck 35 (EORTC QLQ-H&N35) has been in use worldwide as a reliable tool for assessing the QOL in head and neck cancer survivors.⁴⁻⁶ This has been useful in identifying which impairments encountered by the patients affect their daily activities of living the most after treatment. In addition, analysis of the QOL study results can help to identify subgroups of patient who are more likely to be affected and therefore require additional targeted support for recovery.

Methods

Study design

This was a prospective study performed at a single tertiary institution in Singapore with patients recruited between the study period of 01/09/2015 – 06/02/2020. Patients scheduled for major head and neck surgery are seen in a combined outpatient clinic consisting of different members of the healthcare team. The patients were recruited at this point and the initial survey conducted by an advanced practice nurse (APN). The English versions of both questionnaires were used in this study. The APN provided verbal translations for patients who were not English literate. Patients were invited to join the study if they were scheduled for a major elective head and neck surgery. Patients planned for thyroid or salivary gland surgery were only included if the surgery entailed more than resection of the gland with or without lymphatic clearance. Exclusion criterion included patients who subsequently did not undergo surgery, underwent neck dissection alone, benign histology of the resected specimen or patients who were unable to complete the 6-month survey. The study was approved by the local institutional review board.

Two QOL questionnaire tools were employed, namely the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and the Head and Neck Cancer module (EORTC QLQ-H&N35). The survey was carried out by the APN at recruitment as well as at one month and six months after their surgery. The interview was carried out either via face-to-face in the clinic or over the telephone and recorded in a central electronic database. All questions are scored on a 4 point Likert scale. Scores from both questionnaires are then translated to a 0 – 100 points scale as per the scoring manual. Higher scores in the functional and global health status scales indicated towards better levels of functioning whereas higher scores in the symptom scales demonstrated higher levels of symptoms. The scores at diagnosis are presented for use as reference values for future studies. Our study population was then divided into subgroups and evaluated to identify patient, disease or treatment factors that would impact the patients' quality of life post treatment. The QOL scores were also compared against two recent large QOL studies on head and neck cancer survivors, Hammerlid et al (2017) and Liao et al (2019).

This study was approved by the local ethics committee (SingHealth Centralised Institutional Review Board, Reference Number 2018/2950). Consent was obtained from all participants.

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30)

The QLQ-C30 questionnaire is used to measure the QOL for all patients with cancer. It consists of both multi-item and single-item scales. The QLQ-C30 has 30 questions which are divided into five functional scales (physical, social, role, emotional and cognitive functioning), three symptom scales (fatigue, pain and nausea and vomiting), a global health status scale and six single items (dyspnoea, appetite loss, insomnia, constipation, diarrhoea and financial difficulties). A higher score in the global health status or functional scale corresponded with a better level of function. Higher scores in the symptom scales showed more symptoms encountered by the patient.

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Head and Neck 35 (EORTC QLQ-HN35)

The QLQ-HN35 questionnaire is used in assessing the QOL specifically for patients with head and neck cancers. It consists of seven scales (pain, problems with swallowing, senses, speech, social eating, sexuality and social contact) as well as eleven single items (problems with the teeth, mouth opening, dry mouth, sticky saliva, coughing, feeling unwell as well as the use of painkillers, feeding tube, nutritional supplement, loss of weight and weight gain). Higher scores reflect that the patients are more symptomatic.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) considering a p-value ≤ 0.05 and 95% confidence interval. The means and standard deviations (SD) were used for descriptive purposes for continuous parameters. Paired samples T-test was performed for comparison of results across time as well as for comparison with previously published data. The Mann-Whitney U and Kruskal-Wallis tests were used respectively for analyses between two or more categorical groups.

Results

A total of 169 patients were identified and enrolled in the pre-treatment interview during the study period. From the initial number, 4 patients subsequently declined surgery and 4 patients underwent neck dissection alone. 6 patients underwent surgery for non-malignant causes i.e. ameloblastoma. 8 patients dropped out of the study while 7 patients passed away within 6 months for various reasons. A final total of 140 patients was then enrolled into the study.

The study population (Table 1) consisted of 93 (66.4%) male patients and 47 (33.6%) female patients with a mean age of 62 (26 – 88) years. The large majority of the population had oral cancer with 110 (78.6%) cases. Squamous cell carcinoma was the most common cancer throughout the study population with 129 (92.1%) cases. Most of the patients had advanced disease with 22 (15.7%) and 69 (49.3%) patients at stage III and stage IV, respectively. All patients received resection of the primary site. 93 (66.4%) patients had a unilateral neck dissection while 37 (26.4%) had bilateral neck dissection. In addition, 84 (60%) of the patients had a tracheostomy. 74 patients required surgical reconstruction with 67 (47.9%) and 7 (5%) receiving a free or pedicled flap, respectively. 59 (42.1%) patients received radiotherapy alone as adjuvant therapy while 30 (21.4%) patients received both chemotherapy and radiotherapy. The pre-treatment EORTC QLQ-C30 and QLQ-HN35 scores obtained at diagnosis are reported to be used as a reference value for future studies (Table 2 – 4).

Subgroup analysis

The study population was divided into subgroups of patient and disease characteristics as well as extent of treatment received. The global health status (GHS) scores at 6-months post treatment were analyzed across the different subgroups (Table 5). None of the patient or socioeconomic characteristics were found to have a significant impact on the GHS scores. There was no difference in the GHS scores between gender, age groups or social factors. Patients reported a lower GHS score the more extensive the treatment received. For the sake of clarity, the subsequent scores are reported as the mean and standard deviation with the relevant

p-value. Patients who underwent a tracheostomy had a lower score than those who did not [71.4 (15.5) vs 65.6 (14.0), $p<0.01$]. This was also true for patients who required a surgical flap. Patients who did not receive a flap scored higher than those with a free or pedicled flap [71.2 (13.7) vs 65.8 (15.4) vs 57.1 (12.2), $p<0.01$]. Adjuvant treatment was also associated with a lower GHS score ($p<0.01$). The stage of the disease was found to have impacted the patients, with locally advanced disease or a higher AJCC stage associated with lower GHS scores for both ($p<0.01$).

EORTC QLQ-C30

The results of the EORTC QLQ-C30 scores are as published in Table 6. The scores taken at 6 months after treatment were analyzed against the scores at diagnosis. There was no significant difference in the GHS despite the interval since treatment ($p=0.82$). Patients reported a lower physical functional scale after treatment [94.9 (11.0) vs 90.9 (17.2), $p=0.05$]. However, the patients felt emotionally better than at diagnosis [86.0 (15.8) vs 94.6 (11.0), $p<0.01$]. Symptoms wise, the patients reported a significant improvement in pain after treatment [22.3 (23.5) vs 10.7 (16.4), $p=0.03$].

The scores at 6 months after treatment were compared against two recent large studies, Hammerlid (2017) and Liao (2019). Hammerlid et al presented their QOL scores at 3 years post treatment whereas Liao et al evaluated their study population at 6 months post-treatment. Patients at our center reported a lower GHS than both studies [67.9 (14.8) vs 73.2 (21.3), $p=0.02$ vs 70.9 (22.1), $p=0.21$]. However, our patients fared better on the functional scales when compared to the Swedish population (Table 6). Our study population also reported less symptoms than both Hammerlid et al and Liao et al.

EORTC QLQ-HN35

The results of the EORTC QLQ-HN35 are shown in Table 7. Patients reported an improvement in the pain scores after treatment [15.3 (16.1) vs 6.1 (10.3), $p=0.04$]. There was no other significant difference in the symptomology other than an increased need for nutritional supplements [17.1 (37.7) vs 40.7 (49.1), $p=0.01$]. Difficulty swallowing [18.5 (26.3) vs 10.9 (19.6) vs 10.6 (19.7), $p=0.001$] was significantly higher in our patients than with Hammerlid et al and Liao et al. However, our study population fared better with regards to teeth problems [5.0 (14.3) vs 21.4 (32.3) vs 27.8 (33.8), $p<0.01$], coughing [6.9 (14.6) vs 17.3 (24.6) vs 26.0 (33.6), $p<0.01$] or feeling ill [4.0 (14.1) vs 10.8 (20.0) vs 18.6 (29.0), $p<0.01$]. When compared against Hammerlid et al, our patient population reported significantly less symptoms with regards to pain, senses, sexuality, teeth problems, dry mouth, coughing and feeling ill. Unfortunately, our patients reported more difficulties with swallowing [18.5 (26.3) vs 10.9 (19.6), $p=0.01$] and social eating [17.5 (23.9) vs 11.7 (22.6), $p=0.04$]. In comparison with Liao et al, patients generally reported less symptoms except for swallowing as mentioned above.

Discussion

Our study populations reported a lower physical functional score at 6 months after treatment than at diagnosis. However, there was no specific significant changes in the different categories of physical dysfunction. Hammerlid et al demonstrated that patients experience the most deterioration after treatment.

The study also showed that patients showed the most improvement only at one year after treatment.⁷ In a systematic review by Klein J et al looking at 18 studies, chemoradiotherapy was shown to be a factor in the deterioration of the patient's QOL. Klein J et al reported the persistence of poorer QOL scores at 6 months when compared to the pre-treatment scores. These studies reported an improvement in most domains back to baseline only at 1 year after treatment.⁸ Wang K et al also reported that radiotherapy and neck dissection were associated with worse symptoms at 6 months post-treatment especially with pain and mouth opening. These patients reported normalization of the dysfunctions over time.⁹ Similar findings were reflected in our patients' scores especially with over 63% of the study patients still recuperating from adjuvant therapy. A proposed continuation of the study may show a return to baseline at 1 year.

QOL scores were significantly lower the more extensive the disease. Our study has also identified that lower GHS scores are associated with the extent of resection required, tracheostomy creation, surgical flap reconstruction and adjuvant therapy. The main difference post treatment was the increased need for nutritional supplements and is likely due to the persistent dysphagia as noted when compared against Hammerlid et al and Liao et al. Dysphagia, oral pain and xerostomia are a recognized complication from radiotherapy.^{10,11} As the majority of our study population received adjuvant radiotherapy, this would account for the persistent dysphagia and the need for nutritional supplements as reported at the 6 months mark.

The different socioeconomic subgroups were not found to have a difference in outcomes. Contrary to our findings, Liao et al observed that a high socioeconomic status was associated with a better global QOL.⁶ This was similarly reported by Tribius S et al that long term QOL was poorer in patients with a lower socioeconomic background.¹² Janda M et al also observe a similar trend in that higher education levels and being married were associated with greater social and functional wellbeing.¹³ In a study by Gopal KS et al, patients with a lower education level or lower income were noted to have a poorer outcome with a higher cancer mortality rate.¹⁴ The authors postulate that this could be a result of the local health care system which heavily subsidizes the financial costs to allow the general population access to affordable universal health care.

There were several limitations to our study design. The questionnaires were completed by a trained member of the study team after conducting a verbal interview with the patients. In addition, our local population, especially the older generation have a limited proficiency of the English language. In these cases, the interviewer acted as a translator using the English versions of both questionnaire modules. As a result, there exists a potential interviewer bias which could have been avoided with a self-reported approach. Furthermore, there has been a recent revision to the EORTC Head and Neck Module (EORTC QLQ-HN43). This latest edition will likely replace the EORTC QLQ-HN35 as the standard for future QOL studies.¹⁵

Conclusion

The QOL of head and neck cancer survivors is expected to decline in the interim period following surgery. Socioeconomic factors were not found to have a role in the outcomes. Patients experience more dysfunction especially with swallowing and social eating the more extensive the disease and the surgery. Adjuvant chemoradiotherapy was shown to be a contributing factor to the lower QOL. Current literature supports the

findings of an initial decline after treatment with most dysfunctions returning to baseline after approximately a year. Our findings suggest that further rehabilitation targeted towards swallowing will be beneficial for the patients. A continuation of the study with analysis of the QOL scores at 1 year post treatment would be helpful to determine if our head and neck cancer survivors experience the same.

Declarations

Funding

The authors did not receive any support from any organization for the study.

Conflicts of Interest

The authors declares that they have no conflict of interest.

Availability of data and material

Data will be made available via correspondence with the correspondent author.

Code availability

Not applicable

Authors' contribution

Not applicable

Ethics approval

This study was approved by the local ethics committee (SingHealth Centralised Institutional Review Board, Reference Number 2018/2950).

Consent to participate

Written informed consent was obtained from all individual participants at the start of the study

Consent for publication

Not applicable

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Tables

Table 1 Sociodemographic data and disease characteristics

Characteristic	Total	
Age (years)	61.7 (26 – 88)	
Gender		
Male	47	33.6 %
Female	93	66.4 %
Marital status		
Single	15	10.7 %
Married	108	77.1 %
Divorced	13	9.3 %
Widowed	4	2.9 %
Highest education level		
Nil	3	2.1 %
Primary	53	37.9 %
Secondary	43	30.7 %
Tertiary	37	26.4 %
Not available	4	2.9 %
Employment status		
Student	1	0.7 %
Unemployed	56	40.0 %
Part time	9	6.4 %
Full time	68	48.6 %
Not available	6	4.3 %
Monthly income (SGD)		
<1001	35	25.0 %
1001 – 3000	43	30.7 %
3001 – 5000	21	15.0 %
>5000	3	2.1 %
Not available	38	27.1 %
Adverse exposures		
Smoking	47	33.6 %

Alcohol consumption	27	19.3 %
Betel nut chewing	2	1.4 %
Histology		
Squamous cell carcinoma	129	92.1 %
Sarcoma	4	2.9 %
Salivary gland cancers	4	2.9 %
Nasopharyngeal carcinoma	2	1.4 %
Papillary thyroid carcinoma	1	0.7 %
Primary site		
Oral cavity	110	78.6 %
Nasopharynx	2	1.4 %
Oropharynx	1	0.7 %
Hypopharynx	6	4.3 %
Larynx	13	9.3 %
Sinofacial	3	2.1 %
Salivary gland	2	1.4 %
Thyroid	2	1.4 %
Ear	1	0.7 %
Surgical intervention		
Neck dissection – unilateral	93	66.4 %
Neck dissection - bilateral	37	26.4 %
Tracheostomy	84	60.0 %
Flap reconstruction	74	52.9 %
Adjuvant treatment		
None	49	35.0 %
Chemotherapy alone	1	0.7 %
Radiotherapy alone	59	42.1 %
Chemoradiotherapy	30	21.4 %
Unavailable	1	0.7 %
AJCC stage		

I	28	20.0 %
II	21	15.0 %
III	22	15.7 %
IV	69	49.3 %

Table 2 Pre-treatment mean and standard deviation for the EORTC QLQ-C30 and EORTC QLQ-HN35 scores by gender and age

	<u>All</u>	<u>Men</u>	<u>Women</u>	<u>p-value</u>	<u><65 years</u>	<u>≥65 years</u>	<u>p-value</u>
	-	(n=93)	(n=47)	-	(n=86)	(n=54)	-
EORTC QLQ-C30							
Global quality of life	67.4 (16.9)	67.7 (17.1)	66.7 (16.7)	0.63	66.8 (16.9)	68.4 (16.9)	0.42
Physical functioning	94.9 (11.0)	94.2 (11.3)	96.3 (10.6)	0.10	95.7 (10.0)	93.6 (12.6)	0.27
Role functioning	92.1 (16.4)	91.2 (16.6)	94.0 (16.1)	0.17	92.4 (14.4)	91.7 (19.4)	0.58
Emotional functioning	86.0 (15.8)	87.9 (15.2)	82.3 (16.5)	0.02	83.4 (17.4)	90.1 (12.0)	0.03
Cognitive functioning	92.0 (13.9)	91.6 (13.4)	92.9 (15.0)	0.18	93.0 (13.2)	90.4 (15.0)	0.25
Social functioning	92.9 (17.1)	91.5 (19.4)	95.7 (11.2)	0.21	91.3 (20.1)	95.6 (10.4)	0.32
Fatigue	12.8 (17.4)	14.9 (18.9)	8.5 (12.9)	0.05	10.2 (13.8)	16.9 (21.4)	0.09
Nausea and/or vomiting	1.0 (4.4)	1.1 (4.8)	0.7 (3.4)	0.77	0.8 (4.4)	1.2 (4.4)	0.31
Pain	22.3 (23.6)	22.9 (24.6)	20.9 (21.8)	0.83	23.1 (22.7)	21.0 (25.1)	0.38
Dyspnoea	4.8 (13.0)	6.1 (14.7)	2.1 (8.2)	0.10	3.5 (11.5)	6.8 (15.0)	0.12
Insomnia	17.9 (26.0)	18.6 (27.6)	16.3 (22.9)	0.85	18.6 (24.8)	16.7 (28.0)	0.38
Appetite loss	9.8 (20.6)	11.5 (22.8)	6.4 (15.0)	0.26	8.5 (17.8)	11.7 (24.4)	0.61
Constipation	5.0 (30.2)	6.8 (36.3)	1.4 (9.7)	0.15	6.2 (37.4)	3.1 (11.7)	0.74
Diarrhoea	1.0 (6.9)	1.4 (8.4)	0.0 (0.0)	0.22	1.2 (8.0)	0.6 (4.5)	0.84
Financial difficulties	15.5 (47.9)	16.5 (33.6)	13.5 (68.3)	0.12	20.9 (58.8)	6.8 (18.7)	0.19
EORTC QLQ-HN35							
Local pain	15.3 (16.2)	15.9 (16.8)	14.2 (14.8)	0.67	15.2 (14.6)	15.4 (18.5)	0.61
Swallowing	12.4 (17.9)	14.6 (19.5)	8.0 (13.2)	0.05	10.6 (16.7)	15.3 (19.4)	0.18
Senses	5.2	5.6	4.3	0.88	6.5	3.1 (9.2)	0.13

	(13.6)	(14.9)	(10.7)		(15.7)		
Speech	13.1 (23.3)	15.9 (26.2)	7.6 (15.0)	0.11	11.2 (20.4)	16.0 (27.3)	0.62
Social eating	16.6 (22.4)	17.1 (23.1)	15.6 (21.3)	0.67	16.0 (20.9)	17.6 (24.9)	0.86
Social contact	7.4 (15.4)	8.3 (17.3)	5.5 (10.5)	0.76	7.1 (15.7)	7.9 (15.1)	0.88
Sexuality	6.9 (19.2)	5.6 (15.6)	9.6 (24.8)	0.57	7.4 (19.6)	6.2 (18.7)	0.61
Teeth problems	6.0 (15.1)	7.2 (16.9)	3.5 (10.4)	0.27	5.8 (15.5)	6.2 (14.6)	0.70
Opening mouth wide	9.0 (20.7)	10.4 (23.6)	6.4 (13.3)	0.84	8.9 (19.4)	9.3 (22.8)	0.74
Dry mouth	13.8 (19.6)	13.6 (20.4)	14.2 (18.1)	0.64	11.6 (18.3)	17.3 (21.2)	0.10
Sticky saliva	15.5 (22.0)	17.6 (23.9)	11.3 (17.4)	0.18	13.2 (18.6)	19.1 (26.4)	0.29
Coughing	6.2 (17.2)	7.2 (19.6)	4.3 (11.2)	0.74	3.5 (11.5)	10.5 (23.2)	0.05
Feeling ill	2.1 (10.7)	2.5 (12.3)	1.4 (6.8)	0.77	1.9 (7.8)	2.5 (14.3)	0.60
Painkillers	28.1 (45.1)	28.3 (45.3)	27.7 (45.2)	0.94	30.6 (46.4)	24.1 (43.2)	0.41
Nutritional supplements	17.1 (37.8)	17.2 (37.9)	17.0 (38.0)	0.98	17.4 (38.2)	16.7 (37.6)	0.91
Feeding tube	5.7 (23.3)	8.6 (28.2)	0.0 (0.0)	0.04	5.8 (23.5)	5.6 (23.1)	0.95
Weight loss	47.9 (50.1)	48.4 (50.2)	46.8 (50.4)	0.86	50.0 (50.3)	44.4 (50.2)	0.52
Weight gain	3.6 (18.6)	3.2 (17.8)	4.3 (20.4)	0.76	4.7 (21.2)	1.9 (13.6)	0.39

Table 3 Pre-treatment mean and standard deviation for the EORTC QLQ-C30 and EORTC QLQ-HN35 scores by marital and employment status

	<u>No spouse</u>	<u>Spouse</u>	<u>p-value</u>	<u>Unemployed</u>	<u>Employed</u>	<u>p-value</u>
	(n=32)	(n=108)	-	(n=57)	(n=77)	-
EORTC QLQ-C30						
Global quality of life	67.4 (16.9)	64.1 (17.9)	0.38	68.6 (16.7)	67.1 (16.8)	0.63
Physical functioning	94.9 (11.0)	95.0 (8.1)	0.42	93.9 (11.1)	95.3 (11.3)	0.26
Role functioning	92.1 (16.4)	92.2 (15.8)	0.78	90.6 (18.4)	92.6 (15.4)	0.38
Emotional functioning	86.0 (15.8)	89.3 (16.6)	0.07	88.5 (12.8)	84.6 (17.7)	0.44
Cognitive functioning	92.0 (13.9)	92.2 (12.7)	0.81	90.4 (14.4)	92.6 (13.9)	0.12
Social functioning	92.9 (17.1)	91.7 (21.6)	0.91	95.8 (10.2)	90.3 (21.0)	0.15
Fatigue	12.8 (17.4)	13.5 (14.9)	0.48	12.9 (17.3)	13.1 (18.0)	0.88
Nausea and/or vomiting	1.0 (4.4)	0.5 (2.9)	0.58	0.9 (3.8)	1.1 (4.9)	0.85
Pain	22.3 (23.6)	23.4 (25.0)	0.82	19.9 (20.3)	24.2 (26.1)	0.86
Dyspnoea	4.8 (13.0)	3.1 (9.9)	0.49	7.0 (15.1)	3.5 (11.6)	0.14
Insomnia	17.9 (26.0)	18.7 (29.3)	0.96	13.5 (22.6)	22.1 (28.4)	0.09
Appetite loss	9.8 (20.6)	13.5 (23.7)	0.29	6.4 (14.7)	12.6 (24.2)	0.39
Constipation	5.0 (30.2)	2.1 (8.2)	0.93	1.2 (6.2)	7.4 (39.6)	0.33
Diarrhoea	1.0 (6.9)	0.0 (0.0)	0.34	0.6 (4.4)	1.3 (8.4)	0.88
Financial difficulties	15.5 (47.9)	18.7 (34.8)	0.16	15.8 (64.3)	16.5 (33.6)	0.25
EORTC QLQ-HN35						
Local pain	15.3 (16.2)	16.1 (13.2)	0.32	14.3 (14.8)	16.5 (17.5)	0.76
Swallowing	12.4 (17.9)	8.3 (10.8)	0.57	11.7 (16.1)	13.2 (19.0)	0.39
Senses	5.2 (13.6)	5.4 (12.5)	0.74	4.7 (10.3)	5.7 (16.0)	0.92
Speech	13.1 (23.3)	8.3 (19.6)	0.13	13.3 (23.4)	12.3 (21.8)	0.94
Social eating	16.6 (22.4)	16.1 (20.9)	0.79	15.9 (20.8)	17.6 (24.3)	0.88
Social contact	7.4 (15.4)	4.8 (10.5)	0.31	9.2 (19.3)	6.4 (12.3)	0.66
Sexuality	6.9 (19.2)	1.0 (5.9)	0.03	6.4 (18.6)	5.2 (15.6)	0.03
Teeth problems	6.0 (15.1)	5.2 (17.2)	0.37	4.1 (11.0)	7.8 (17.8)	0.34
Opening mouth wide	9.0 (20.7)	8.3 (20.7)	0.68	5.3 (13.8)	12.1 (24.7)	0.37
Dry mouth	13.8 (19.6)	10.4 (15.7)	0.38	17.0 (19.0)	12.1 (20.2)	0.11
Sticky saliva	15.5 (22.0)	11.5 (16.1)	0.41	17.5 (22.8)	14.7 (22.0)	0.36

Coughing	6.2 (17.2)	3.1 (9.9)	0.39	7.0 (19.7)	4.8 (14.0)	0.30
Feeling ill	2.1 (10.7)	3.1 (17.7)	0.61	1.8 (13.2)	2.2 (8.3)	0.20
Painkillers	28.1 (45.1)	31.3 (47.1)	0.65	21.1 (41.1)	34.2 (47.8)	0.21
Nutritional supplements	17.1 (37.8)	21.9 (42.0)	0.42	21.1 (41.1)	15.6 (36.5)	0.37
Feeding tube	5.7 (23.3)	3.1 (17.7)	0.47	3.5 (18.6)	7.8 (27.0)	0.48
Weight loss	47.9 (50.1)	46.9 (50.7)	0.90	50.9 (50.4)	46.8 (50.2)	0.69
Weight gain	3.6 (18.6)	6.3 (24.6)	0.35	3.5 (18.6)	3.9 (19.5)	0.89

Table 4 Pre-treatment mean and standard deviation for the EORTC QLQ-C30 and EORTC QLQ-HN35 scores by site

	<u>Total</u>	<u>Oral cavity</u>	<u>Larynx</u>	<u>Hypopharynx</u>	<u>Sinofacial</u>	<u>p-value</u>
	(n=132)	(n=110)	(n=13)	(n=6)	(n=3)	-
EORTC QLQ-C30						
Global quality of life	67.1 (17.1)	67.6 (16.9)	63.5 (14.2)	65.3 (29.1)	69.4 (12.7)	0.74
Physical functioning	94.8 (11.3)	95.5 (11.2)	90.3 (11.7)	90.0 (13.8)	97.8 (3.8)	0.28
Role functioning	91.9 (16.7)	93.3 (15.2)	79.5 (24.7)	94.4 (13.6)	88.9 (19.2)	0.08
Emotional functioning	86.0 (15.7)	85.1 (16.0)	92.3 (9.3)	84.7 (21.4)	94.4 (9.6)	0.33
Cognitive functioning	91.7 (14.2)	92.6 (13.7)	89.7 (10.8)	80.6 (26.7)	88.9 (9.6)	0.48
Social functioning	92.7 (17.4)	94.0 (15.1)	88.5 (17.2)	83.3 (40.8)	83.3 (28.9)	0.34
Fatigue	13.3 (17.7)	11.5 (16.8)	21.4 (16.6)	27.8 (25.1)	14.8 (25.7)	0.19
Nausea and/or vomiting	1.0 (4.5)	0.5 (2.7)	2.6 (6.3)	8.3 (13.9)	0.0 (0.0)	0.06
Pain	23.4 (23.8)	25.6 (23.9)	14.1 (23.4)	11.1 (20.2)	5.6 (9.6)	0.04
Dyspnoea	5.1 (13.3)	3.0 (9.6)	12.8 (16.9)	22.2 (34.4)	11.1 (19.2)	0.08
Insomnia	18.4 (26.2)	17.3 (24.6)	25.6 (33.8)	27.8 (39.0)	11.1 (19.2)	0.74
Appetite loss	10.1 (21.0)	10.6 (21.1)	7.7 (20.0)	11.1 (27.2)	0.0 (0.0)	0.87
Constipation	2.8 (11.7)	1.8 (9.9)	2.6 (9.2)	22.2 (27.2)	0.0 (0.0)	<0.01
Diarrhoea	1.0 (7.1)	0.3 (3.2)	2.6 (9.2)	11.1 (27.2)	0.0 (0.0)	0.34
Financial difficulties	16.4 (49.2)	16.1 (52.0)	7.7 (14.6)	38.9 (49.1)	22.2 (38.5)	0.62
EORTC QLQ-HN35						
Local pain	16.2 (16.2)	17.2 (16.9)	10.9 (11.0)	12.5 (12.6)	11.1 (12.7)	0.10
Swallowing	12.8 (18.2)	10.6 (14.8)	25.6 (31.6)	27.8 (25.1)	8.3 (8.3)	0.31
Senses	5.2 (13.7)	3.7 (9.7)	11.5 (18.5)	5.6 (8.6)	33.3 (57.7)	0.18

Speech	13.5 (23.5)	8.5 (16.3)	57.3 (32.3)	16.7 (23.0)	0.0 (0.0)	<0.01
Social eating	17.4 (22.8)	17.7 (22.7)	21.2 (26.0)	12.5 (22.8)	0.0 (0.0)	0.43
Social contact	7.8 (15.8)	6.1 (14.2)	21.0 (20.0)	11.1 (24.1)	6.7 (6.7)	0.05
Sexuality	7.1 (19.5)	5.9 (18.1)	11.5 (30.0)	16.7 (18.3)	11.1 (19.2)	0.34
Teeth problems	6.1 (15.3)	6.7 (16.2)	5.1 (12.5)	0.0 (0.0)	0.0 (0.0)	0.80
Opening mouth wide	9.6 (21.2)	11.2 (22.7)	0.0 (0.0)	0.0 (0.0)	11.1 (19.2)	0.47
Dry mouth	13.4 (19.3)	13.9 (19.4)	12.8 (21.7)	11.1 (17.2)	0.0 (0.0)	0.27
Sticky saliva	15.7 (22.3)	14.2 (20.4)	28.2 (35.6)	16.7 (18.3)	11.1 (19.2)	0.92
Coughing	6.3 (17.5)	3.0 (10.6)	28.2 (35.6)	22.2 (27.2)	0.0 (0.0)	<0.1
Feeling ill	2.3 (11.0)	1.2 (6.3)	10.3 (28.5)	5.6 (13.6)	0.0 (0.0)	0.67
Painkillers	28.2 (45.2)	30.3 (46.2)	15.4 (37.6)	33.3 (51.6)	0.0 (0.0)	0.49
Nutritional supplements	15.9 (36.7)	16.4 (37.2)	15.4 (37.6)	0.0 (0.0)	33.3 (57.7)	0.25
Feeding tube	5.3 (22.5)	2.7 (16.4)	23.1 (43.9)	16.7 (40.8)	0.0 (0.0)	<0.01
Weight loss	48.5 (50.2)	50.0 (50.2)	53.8 (51.9)	33.3 (51.6)	0.0 (0.0)	0.31
Weight gain	3.8 (19.2)	3.6 (18.8)	0.0 (0.0)	0.0 (0.0)	33.3 (57.7)	0.37

Table 5 Comparison of global health status at 6 months post treatment by subgroups

<u>Subgroup</u>	<u>Mean</u>	<u>SD*</u>	<u>p-value</u>
Gender			
Female	67.9	17.4	0.84
Male	67.9	13.3	
Age (years)			
< 65	68.4	16.5	0.31
≥ 65	67.1	21.8	
Marital status			
Single	70.0	14.0	0.16
Married	66.7	15.2	
Divorced	73.1	13.7	
Widowed	75.0	9.6	
Education level			
Nil	72.2	9.6	0.87
Primary	67.6	14.0	
Secondary	66.9	18.1	
Tertiary	69.6	12.9	
Employment status			
Unemployed	68.2	15.6	0.8
Part time	64.8	16.6	
Full time	68.6	14.0	
Monthly gross salary (SGD*)			
<1001	65.7	15.0	0.23
1001 - 3000	65.5	16.4	
3001 - 5000	74.2	13.2	
>5000	72.2	9.6	
Primary Site			
Oral cavity	68.6	14.8	0.6
Hypopharynx	70.8	7.0	
Larynx	65.4	17.3	

Sinofacial	63.9	21.0	
Neck dissection			
None	69.2	15.8	0.53
Unilateral	69.0	14.3	
Bilateral	65.1	15.8	
Tracheostomy			
None	71.4	15.5	<0.01
Yes	65.6	14.0	
Surgical reconstruction			
None	71.2	13.7	<0.01
Free flap	65.8	15.4	
Pedicled flap	57.1	12.2	
Adjuvant treatment			
None	73.8	12.8	<0.01
Radiotherapy alone	63.9	13.0	
Chemoradiotherapy	65.2	17.8	
Cancer stage – T			
1	75.2	13.7	<0.01
2	69.7	9.7	
3	60.6	19.6	
4	64.4	14.0	
AJCC* stage			
I	76.8	13.3	<0.01
II	69.8	10.7	
III	64.8	18.0	
IV	64.7	14.2	
<i>SD</i> Standard deviation, <i>SGD</i> Singapore dollar, <i>AJCC</i> American Joint Committee on Cancer			

Table 6 Comparison of EORTC QLQ-C30 scores across time and against previously published data on head and neck cancer survivors

	Scores at diagnosis (n=140)		Scores at 6 months (n=140)			Hammerlid 2017 (n = 133)			Liao 2019 (n=127)		
	<u>Mean (SD).</u>		<u>Mean (SD).</u>		<u>p-value*</u>	<u>Mean (SD).</u>		<u>p-value</u>	<u>Mean (SD).</u>		<u>p-value</u>
EORTC QLQ-C30											
Global quality of life	67.4	16.8	67.9	14.8	0.82	73.2	21.3	0.02	70.9	22.1	0.21
Physical functioning	94.9	11.0	90.9	17.2	0.05	85.6	21.2	0.02	90.7	16.8	0.91
Role functioning	92.1	16.4	91.8	16.2	0.87	83.3	30.1	<0.01	95.9	16.6	0.04
Emotional functioning	86.0	15.8	94.6	11.0	<0.01	85.0	18.7	<0.01	88.7	15.9	<0.01
Cognitive functioning	92.0	13.9	88.6	17.3	0.11	86.0	22.2	0.29	84.3	16.7	0.04
Social functioning	92.9	17.1	90.6	16.7	0.31	87.0	16.5	0.07	94.0	14.8	0.08
Fatigue	12.8	17.3	10.7	16.8	0.70	22.8	22.9	<0.01	15.8	22.3	0.04
Nausea and/or vomiting	1.0	4.4	2.0	8.6	0.86	3.1	9.0	0.31	2.4	7.8	0.74
Pain	22.3	23.5	10.7	16.4	0.03	14.9	20.7	0.07	15.0	21.9	0.08
Dyspnoea	4.8	13.0	4.5	13.9	0.97	17.8	23.9	<0.01	6.0	17.0	0.43
Insomnia	17.9	25.9	12.1	20.0	0.35	18.8	26.4	0.02	19.4	30.7	0.02
Appetite loss	9.8	20.5	9.5	19.2	0.97	11.7	25.1	0.42	11.0	23.0	0.57
Constipation	5.0	30.1	1.4	6.8	0.56	3.8	11.4	0.04	11.3	20.2	<0.01
Diarrhoea	1.0	6.8	1.2	7.4	0.97	10.8	21.9	<0.01	5.5	16.7	0.01
Financial difficulties	15.5	47.7	13.3	25.8	0.79	11.6	25.2	0.57	8.1	18.7	0.06
*Comparison of scores at 6 months post treatment versus diagnosis. Comparison of scores at 6 months versus previously published data											

Table 7 Comparison of EORTC QLQ-HN35 scores across time and against previously published data on head and neck cancer survivors

	Scores at diagnosis (n=140)		Scores at 6 months (n=140)			Hammerlid 2017 (n = 133)			Liao 2019 (n=127)		
	<u>Mean (SD).</u>		<u>Mean (SD).</u>		<u>p-value*</u>	<u>Mean (SD).</u>		<u>p-value</u> ☒	<u>Mean (SD).</u>		<u>p-value</u> ☒
	-		-		-	-		-	-		-
EORTC QLQ-HN35											
Local pain	15.3	16.1	6.1	10.3	0.04	14.5	19.8	<0.01	8.1	16.5	0.23
Swallowing	12.4	17.8	18.5	26.3	0.34	10.9	19.6	0.01	10.6	19.7	0.01
Senses	5.2	13.5	11.4	21.4	0.33	20.5	27.4	<0.01	12.2	21.9	0.77
Speech	13.1	23.2	13.3	20.0	0.98	12.1	19.1	0.62	11.3	19.5	0.41
Social eating	16.6	22.3	17.5	23.9	0.88	11.7	22.6	0.04	14.9	25.0	0.39
Social contact	7.4	15.3	8.4	15.1	0.84	7.6	14.7	0.64	6.5	15.1	0.28
Sexuality	6.9	19.1	10.6	22.8	0.61	28.8	36.3	<0.01	13.7	37.5	0.43
Teeth problems	6.0	15.0	5.0	14.3	0.88	21.4	32.3	<0.01	27.8	33.8	<0.01
Opening mouth wide	9.0	20.6	19.3	24.6	0.08	17.6	29.3	0.61	27.8	33.8	0.02
Dry mouth	13.8	19.5	21.7	22.5	0.13	47.3	36.3	<0.01	21.3	33.5	0.91
Sticky saliva	15.5	22.0	20.2	22.1	0.36	18.6	28.4	0.60	35.2	34.7	<0.01
Coughing	6.2	17.2	6.9	14.6	0.90	17.3	24.6	<0.01	26.0	33.6	<0.01
Feeling ill	2.1	10.7	4.0	14.1	0.79	10.8	20.0	<0.01	18.6	29.0	<0.01
Painkillers	28.1	44.9	23.6	42.4	0.64						
Nutritional supplements	17.1	37.7	40.7	49.1	0.01						
Feeding tube	5.7	23.2	17.9	43.5	0.25						
Weight loss	47.9	50.0	37.1	48.3	0.23						
Weight gain	3.6	18.6	3.6	18.6	1.00						
*Comparison of scores at 6 months post treatment versus diagnosis. ☒Comparison of scores at 6 months versus previously published data											