# Impact of treatment modalities on oral cancer patients' health-related quality of life over a time trajectory

**Jennifer Geraldine Doss[1,2]^, William Murray Thomson[3]^, Bernadette K. Drummond[4]^, Wan Maria Nabillah Ghani[1]^**

[1]Oral Cancer Research & Coordinating Centre, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia; [2]Department of Community Oral Health & Clinical Prevention, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia; [3]Sir John Walsh Research Institute, School of Dentistry, University of Otago, Dunedin, New Zealand; [4]Paediatric Dentistry, School of Dentistry, Worsley Building, Clarendon Way, University of Leeds, Leeds, UK

*Contributions:* (I) Conception and design: JG Doss, WM Thomson, BK Drummond; (II) Administrative support: WMN Ghani; (III) Provision of study materials or patients: JG Doss; (IV) Collection and assembly of data: JG Doss; (V) Data analysis and interpretation: JG Doss; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* Jennifer Geraldine Doss. Oral Cancer Research & Coordinating Centre, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia; Department of Community Oral Health & Clinical Prevention, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia. Email: jendoss@um.edu.my.

**Background:** The aim of this study was to assess the impact of oral cancer and its related treatment on patients' health-related quality of life (HRQoL) and to identify factors associated with HRQoL change over time.

**Methods:** This was a longitudinal observational multi-centre study of a cohort of newly diagnosed oral cancer patients selected using consecutive convenience sampling and followed through over a period of 3 months; from the point of diagnosis (baseline) until 3 months after treatment had commenced. Seven hospital-based oral surgery clinics managing oral cancer patients throughout Malaysia were chosen as sampling points. Data was collected through a face-to-face structured interview in a clinical setting at 3 time points using the translated and cross-culturally adapted and validated FACT-HN (v 4.0) instrument. Six derivatives of FACT summary scores were used to assess HRQoL changes using repeated measures analysis. Multivariate analysis was used to assess the predictors of HRQoL change from baseline to second follow-up visit. Ethics approval was obtained from the Medical Ethics Committee at the Faculty of Dentistry, University of Malaya.

**Results:** A baseline sample of 76 oral cancer patients was recruited. A high attrition rate (19%—first follow-up; 25%—second follow-up) meant that only a cohort of 42 patients were interviewed from baseline through to the second follow-up at 3 time points (before treatment, 1 month and 3 months after commencing treatment). Oral cancer patients' HRQoL had deteriorated by the first month after commencing treatment and gradually improved, to either close to or better than pre-treatment levels. Surgical intervention produced a greater improvement in patients' overall HRQoL (at 1- and 3-month after commencing treatment) over the other treatment modalities. There was an interaction between tumor size and type of treatment received by patients in respect of their change in HRQoL from baseline to the third month after commencing treatment.

**Conclusions:** Surgery and other treatment modalities impact oral cancer patients' HRQoL differently over time. Notably, interaction between clinical factors, namely tumor size and type of treatment was associated with HRQoL change from pre-treatment till 3 months after commencing treatment. These findings can provide an insight for clinicians in their treatment planning and decision-making for both treatment modalities.

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^ ORCID: Jennifer Geraldine Doss, 0000-0003-2511-7523; William Murray Thomson, 0000-0003-0588-6843; Bernadette K. Drummond, 0000-0002-5786-5879; Wan Maria Nabillah Ghani, 0000-0002-6782-558X.

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## Introduction

Cancer affects a person's quality of life. There is an abundance of evidence from the last four decades showing how a person's quality of life can be severely compromised in terms of their functional, physical, psychological, emotional and social aspects. Oral cancer sufferers are no different. In fact, considering the important functional role of the oral cavity and its related structures, the effects of this disease can be even more debilitating (1-5). The impeding of basic functions such as speech and eating, as well as its implications for socializing, self-esteem and self-confidence, poses a serious challenge (6-11). It is a daily struggle for oral cancer patients to cope with these compromised functions, which healthy individuals take for granted. Upon looking at their plight, we often wonder why they need to go through such painful suffering, but the reasons elude us.

It has been acknowledged that oral cancer is a major public health problem globally, especially in the Asian continent. In Malaysia, based on GLOBOCAN 2020 data, lip and mouth cancer was ranked as the 19th most common cancer in the population, and it is the sixth most common among Malaysian Indian females (12). Oral cancer has one of the lowest survival rates and the important determinant factors for survival are diagnostic delay and ineffective treatment at advanced stages of cancer.

Managing oral cancer is a lifelong and challenging process. A delicate balance between arresting the progression of disease and not compromising the patient's quality of life remains the biggest challenge in treatment decisions. In applying this principle while managing patients, the specialist has a responsibility to include each patient's perceptions and opinions before making a decision on the best treatment regime. More often than not, patients are willing to accept a reduced lifespan instead of compromising their quality of life drastically, especially in terms of speech, eating and swallowing (13). This suggests that some people would choose to risk having fewer years of life in order to maintain what they perceive as a better quality of life. Thus, understanding and appreciating the functional, socio-psychological and physical effects of this disease would further assist healthcare specialists in appreciating the value that oral cancer sufferers attach to different aspects of their health-related quality of life (HRQoL). In cognisant of this, HRQoL data from the patient's perspective is of importance and has become a vital source of information for head and neck cancer treatment outcomes (14-18).

In Malaysia, such information is lacking and the condition is still silently borne by patients. There is therefore an urgent need for Malaysian specialists to be better informed about how their oral cancer patients view their on-going HRQoL at different intervals of their life, especially upon diagnosis and, before and after commencing different treatment modalities (19). This information would indeed be relevant and useful for specialists when making decisions during the course of managing such patients. This study aims to assess the impact of oral cancer and its related treatment on patients' HRQoL; and to identify factors associated with (and predictors of) HRQoL among Malaysian oral cancer patients. We hypothesize that surgery impacts oral cancer patients HRQoL differently from other treatment modalities. We present the following article in accordance with the STROBE reporting checklist (available at https://fomm.amegroups.com/article/view/10.21037/fomm-21-90/rc).

## Methods

### *Study design*

This was a longitudinal multi-centre study of a cohort of oral cancer patients over a period of 3 months, from the point of diagnosis (baseline) until 3 months after treatment had commenced.

Sample size was determined by the availability of newly diagnosed oral cancer patients who attended the specified oral surgery specialist clinics over the recruitment period. Seven oral surgery specialist clinics throughout Malaysia were chosen to be the sampling points. These included four hospitals in the peninsular west coast, two hospitals in the peninsular east coast and two hospitals in East Malaysia. These hospitals were chosen based on the premise that most oral cancer patients in those regions were referred and managed there.

Consecutive convenience sampling was used, whereby all patients with oral cancer seen at the seven participating hospitals during a 5-month recruitment period was invited to participate in this study. Inclusion criteria was adults aged 18 years old and above who were newly diagnosed with oral cancer and had yet to start any treatment. Participants included in-patients and out-patients, with disease staging ranging from I to IV. Mentally incoherent patients were excluded from this study.

### *Data collection*

Data were collected through face-to-face structured interview using the translated and cross-culturally adapted Functional Assessment of Cancer Therapy – Head & Neck (FACT-HN) (v 4.0) instrument (19). The FACT sub-scale scores comprised physical (PWB), social (SWB), emotional (EWB), functional (FWB), head and neck (HNSC) and Malaysian added questions (MAQ). Six derivatives FACT summary scores were used to assess HRQoL namely FACT-G, FACT-HN, FACT-HN (TOI), FACT-HNSI, FACT-HNSI (MAQ) and FACT-HN (MAQ). Data collection was done at 3 time points for each patient. These time points were:

(I) Visit 1: 1–2 weeks after diagnosis (baseline);
(II) Visit 2: 1 month after commencement of treatment (first follow-up);
(III) Visit 3: 3 months after commencement of treatment (second follow-up).

Although these data collection points were specified, a time allowance of 1 week before or after each time point was allowed for in carrying out the interviews. This was done to accommodate any unforeseen circumstances that could have been encountered (including condition of patients) in doing the interviews.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethical approval for this study was obtained from the Faculty of Dentistry Medical Ethics Committee, University of Malaya [No. DF 0306/001/(L)]. Patient information sheet was given to patients and informed consent was obtained prior to data collection.

### *Statistical analysis*

Data were analysed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA). Descriptive statistics [mean (SD)] was used to describe the FACT summary and subscale scores at baseline, first follow-up and second follow-up visits. The outcome of this study was HRQoL mean change. Predictors were patient's sociodemographic and clinical details. In order to calculate the mean change in patients' HRQoL from baseline to second follow-up visit, repeated measures analysis was used. Paired *t*-test was conducted to assess the significance of this HRQoL mean change. The significance level was set at P value <0.05.

Multivariate analysis was used to assess the association between patients' socio-demographic characteristics and clinical details with the change in their HRQoL from baseline to second follow-up visit. A factor was deemed to be associated with the HRQoL outcome when the P value was less than 0.05, the Partial Eta Square value was more than 0.15, and the power of the test was more than 80%, indicating that the type II error was less than 20%. Levene's Test of Equality of Variances (LTEV) was then used to assess whether variances were equal. When the P value was more than 0.05, equal variance was assumed and the Bonferroni Multiple Comparison (BMC) post-hoc test was used to determine the difference among mean scores within the factor. However, where the P value was less than 0.05, equal variances was not assumed and Dunnett's T3 (DUNT3) post-hoc test was used instead. The association of factors with each HRQoL outcome is explained in terms of its main effect and any interactions which were observed.

## Results

A total of 76 patients with cancer of the oral cavity were recruited at baseline. However, only 42 patients were successfully followed until the second follow-up visit. This paper will report only on the findings obtained from the cohort of patients who were followed up for all three visits.

*Table 1* shows the sociodemographic and clinical characteristics of sample at baseline. The ratio of females to males was 2:1, with majority being above 50 years old. Two-thirds of patients had cancer at the buccal mucosa and tongue, and 60% patients were diagnosed at advanced stages.

Data on the overall impact of oral cancer and related treatment on patients' HRQoL from baseline through the two follow-ups are presented in *Table 2*. The emotional well-being of these patients was found to be significantly better at second follow-up than at baseline (P=0.048), whereas in contrast their functional well-being decreased significantly at first follow-up (P=0.021), after

**Table 1** Sociodemographic characteristics and clinical details of patients at baseline (n=42)

| Characteristics | N (%) |
|---|---|
| Sociodemographic characteristics | |
| Gender | |
| Male | 14 (33.3) |
| Female | 28 (66.7) |
| Age group | |
| 21–49 years | 8 (19.0) |
| 50–64 years | 22 (52.4) |
| 65–87 years | 12 (28.6) |
| Race | |
| Malay | 10 (23.8) |
| Chinese | 8 (19.0) |
| Indian | 19 (45.2) |
| Other | 5 (11.9) |
| Education | |
| None | 12 (28.6) |
| Primary | 18 (42.9) |
| Higher | 12 (28.6) |
| Employment | |
| Employed | 13 (31.0) |
| Unemployed | 29 (69.0) |
| Home life | |
| Married | 25 (59.5) |
| Single | 2 (4.8) |
| Widowed | 15 (35.7) |
| Religion | |
| Muslim | 15 (35.7) |
| Hindu | 18 (42.9) |
| Christian | 2 (4.8) |
| Buddhist | 7 (16.7) |
| Other | 0 (0.0) |
| Clinical characteristics | |
| Tumor site | |
| Lip | 4 (9.5) |
| Buccal mucosa | 15 (35.7) |
| Tongue | 13 (31.0) |
| Jaw bone | 2 (4.8) |
| Palate | 4 (9.5) |
| Other | 4 (9.5) |
| Tumor type | |
| SCC | 41 (97.6) |
| Other | 1 (2.4) |
| Tumor size | |
| 0–2 cm | 6 (14.3) |
| >2–4 cm | 23 (54.8) |
| >4–6 cm | 8 (19.0) |
| >6 cm | 5 (11.9) |
| Cancer staging | |
| Stage I | 8 (19.0) |
| Stage II | 9 (21.4) |
| Stage III | 13 (31.0) |
| Stage IV | 12 (28.6) |
| Treatment type | |
| S | 27 (64.3) |
| Others | 15 (35.7) |
| R | 3 (7.1) |
| C | 0 (0.0) |
| S and R | 8 (19.0) |
| S and C | 1 (2.4) |
| Palliative | 3 (7.1) |

SCC, squamous cell carcinoma; S, surgery; R, radiotherapy; C, chemotherapy.

commencement of treatment. The mean scores for head and neck subscale were found to be significantly higher at baseline compared to at first follow-up (P=0.050) and second follow-up (P=0.008). Overall, HRQoL of oral cancer patients became worse than baseline during first follow-up, which then improved by the second follow-up. This mean change was found to be statistically significant for the FACT-HN (P=0.008) and FACT-HN (TOI) (P=0.017) summary scores.

**Table 2** FACT summary and subscale scores at baseline, first follow-up and second follow-up (n=42)

| Scale | No of items | Possible range of scores | Baseline, mean (SD) | First follow-up, mean (SD) | Second follow-up, mean (SD) |
|---|---|---|---|---|---|
| FACT summary scores | | | | | |
| FACT-G | 27 | 0–108 | 72.9 (14.8) | 70.0 (15.9) | 73.5 (16.6) |
| FACT-HN | 36 | 0–144 | 94.1 (17.6) | 87.3 (20.0) | 91.4 (20.9)[d] |
| FACT-HN (TOI) | 23 | 0–92 | 58.4 (13.9) | 50.1 (15.6) | 53.1 (15.9)[e] |
| FACT-HNSI | 10 | 0–40 | 25.5 (5.9) | 24.1 (6.6) | 25.1 (7.0) |
| FACT-HNSI (MAQ) | 16 | 0–64 | 43.1 (8.4) | 42.9 (9.3) | 43.7 (10.3) |
| FACT-HN (MAQ) | 43 | 0–172 | 113.0 (19.0) | 107.6 (22.5) | 111.6 (24.1) |
| FACT subscale scores | | | | | |
| PWB | 7 | 0–28 | 21.4 (4.9) | 19.6 (6.1) | 19.9 (5.8) |
| SWB | 7 | 0–28 | 20.0 (3.6) | 20.3 (3.6) | 20.3 (3.8) |
| EWB | 6 | 0–24 | 15.6 (4.1) | 17.0 (4.2) | 18.1 (4.5)[a] |
| FWB | 7 | 0–28 | 15.9 (6.7) | 12.8 (6.9) | 15.2 (7.3)[b] |
| HNSC | 9 | 0–36 | 21.2 (4.9) | 17.6 (5.2) | 18.0 (5.9)[c] |
| MAQ | 7 | 0–28 | 18.9 (4.0) | 20.2 (3.4) | 20.1 (4.5) |

[a], pairwise difference between baseline and second follow-up FACT score (P=0.048). [b], pairwise difference between first follow-up and baseline FACT score (P=0.021); first follow-up and second follow-up FACT score (P=0.002). [c], pairwise difference between baseline and first follow-up FACT score (P=0.050); baseline and second follow-up FACT score (P=0.008). [d], pairwise difference between baseline and first follow-up FACT score (P=0.008). [e], pairwise difference between baseline and first follow-up FACT score (P=0.017). MAQ, Malaysian added questions; PWB, physical; SWB, social; EWB, emotional; FWB, functional; HNSC, head and neck.

*Figure 1* compares the impact of surgical intervention to other treatment interventions on patients' FACT summary scores from baseline up until the second follow-up. There were statistically significant differences in the impact of treatment type on patients' HRQoL for all six FACT summary scores. A consistent pattern was observed whereby, among patients receiving surgical interventions, their HRQoL declined by 1 month after commencement of treatment, which then improved significantly by the 3-month post-operation follow-up visit. By contrast, the HRQoL of those receiving other types of treatment interventions (for example, radiotherapy, chemotherapy and combination treatment modalities) continued to deteriorate during that 3-month post-operation period. The greatest difference was observed with the FACT-HNSI, FACT-G and FACT-HN mean scores.

The impact of surgical intervention and other treatment interventions on patients' FACT subscale scores from baseline to second follow-up visit is shown in *Figure 2*. Significant differences were observed in the impacts of either treatment type on HRQoL for three FACT subscales, namely physical (P=0.012) and functional (P=0.022) well-being, and the set of Malaysian questions (P=0.006). The observed pattern for physical and functional impacts among those surgically treated, were almost similar. Patients who underwent surgical interventions experienced a significant improvement in HRQoL by the 3-month follow-up, in contrast to those who received other treatment types. Although patients' emotional well-being had improved with surgical interventions than other treatment types (by the 3-month follow-up), this difference was not found to be statistically significant. The impacts of both treatment types on the social well-being of patients were contrasting; however, the difference was not statistically significant.

*Figure 3* illustrates patients' self-rated HRQoL from baseline until the second follow-up visit. The proportion of patients who self-rated their HRQoL as poor/very poor increased at the first follow-up; however, the proportion of patients reporting having poor HRQoL dropped by the second follow-up visit. In contrast, the proportion of patients who self-rated their HRQoL as being average or good/very good decreased at the first follow-up, however

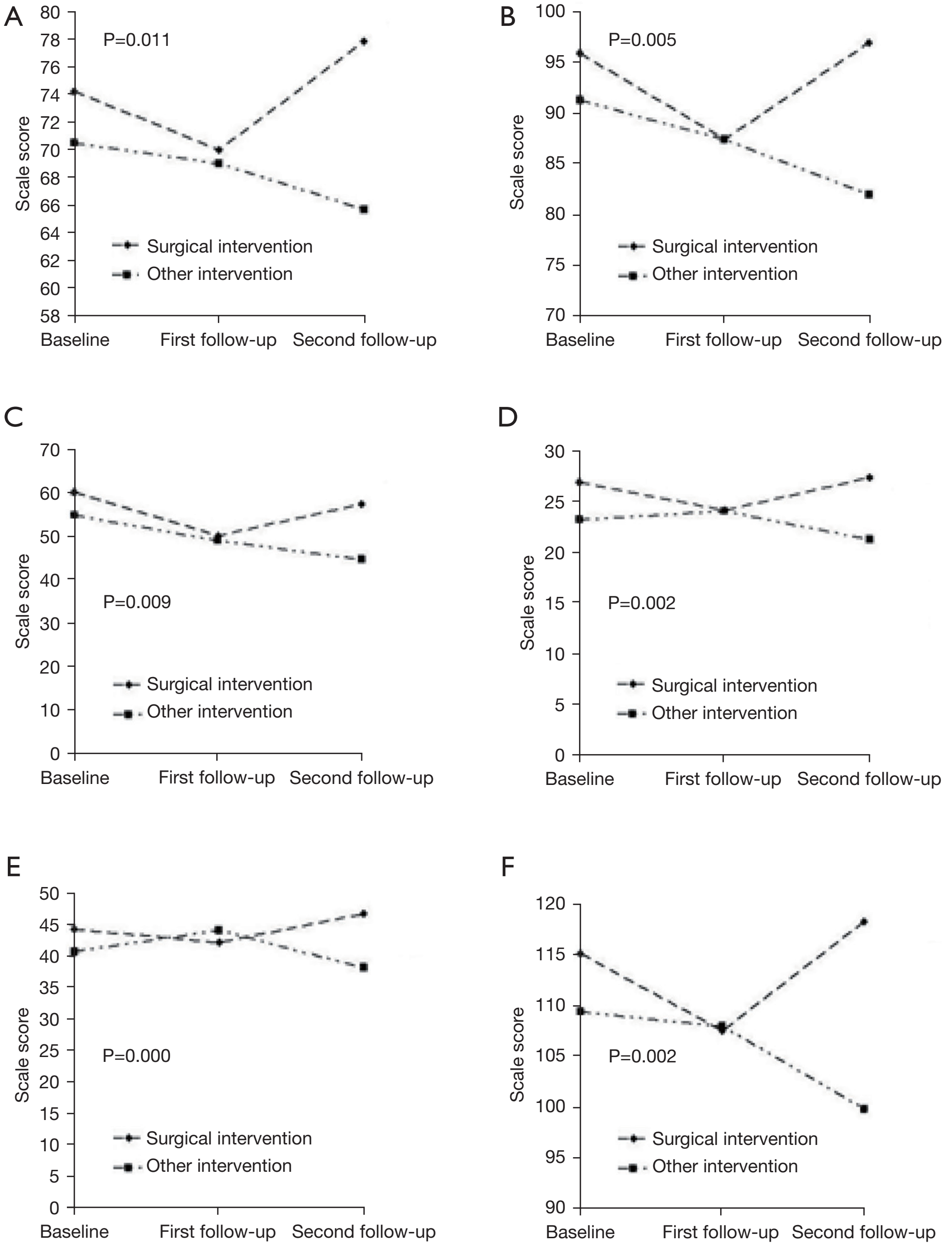

**Figure 1** FACT summary mean scores by treatment modalities from baseline to second follow-up for (A) FACT-G, (B) FACT-HN, (C) FACT-HN (TOI), (D) FACT-HNSI, (E) FACT-HNSI (MAQ), (F) FACT-HN (MAQ). MAQ, Malaysian added questions.

this proportion of patients reporting having average and good HRQoL then increased by the second follow-up.

Next, the data were analysed to identify socio-demographic and clinical factors that were associated with HRQoL change. It was evident that none of the individual socio-demographic or clinical factors affected the HRQoL change observed in patients between baseline and the second follow-up visit (data not shown). However, based on the P value, partial eta squared and observed power values, there was evidence of an interaction between the clinical factors of tumor size and treatment type, which was associated with the mean change score in four of the FACT summary scales, namely the FACT-HN (P=0.022), FACT-HN (TOI) (P=0.045), FACT-HNSI (P=0.040) and FACT-

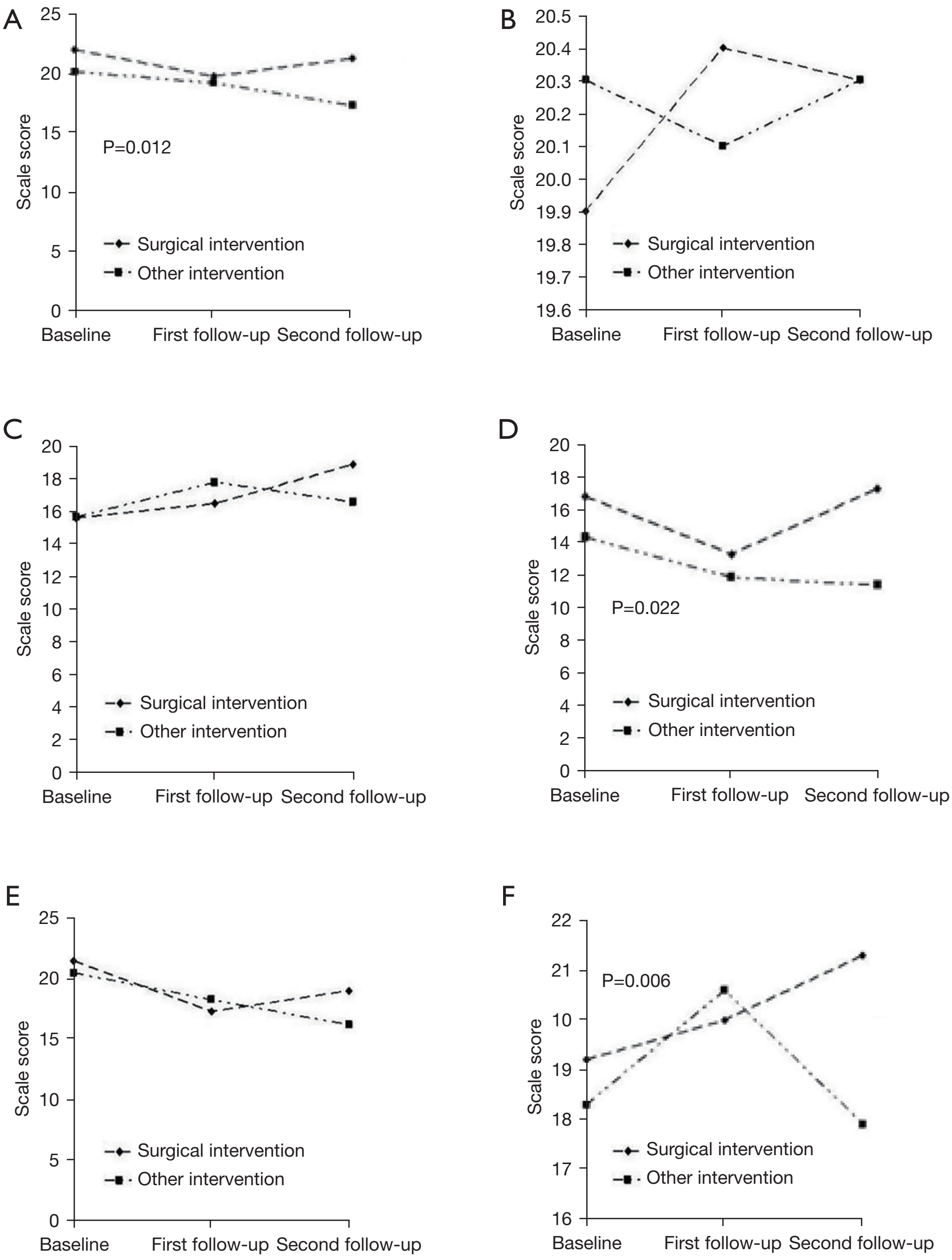

**Figure 2** FACT subscale mean scores by treatment modalities from baseline to second follow-up for (A) PWB, (B) SWB, (C) EWB, (D) FWB, (E) HNSC, (F) MAQ. PWB, physical; SWB, social; EWB, emotional; FWB, functional; HNSC, head and neck; MAQ, Malaysian added questions.

HN (MAQ) (P=0.019) (*Table 3*). This association is further illustrated in *Figure 4*. By contrast, there was no interaction between factors influencing the FACT-G and FACT-HNSI (MAQ) mean change scores between baseline and the second follow-up visit.

*Figure 4* shows the interaction between tumor size and the type of treatment in affecting FACT-HN, FACT-HN (TOI) and FACT-HN (MAQ) overall mean change score from baseline to second follow-up. Generally, large tumors (>6 cm) treated with radiotherapy were associated with smaller declines in FACT-HN, FACT-HN (TOI) and FACT-HN (MAQ) scores, whereas patients with large

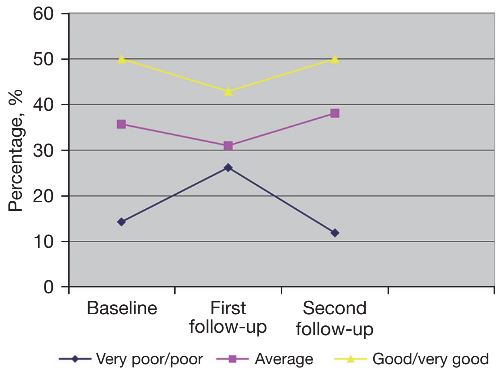

**Figure 3** Patients' global self-rated HRQoL from baseline to second follow-up. HRQoL, health-related quality of life.

tumors receiving palliative care or alternative treatment were associated with larger negative mean change scores. By contrast, patients with small tumors (0–2 cm) who were treated with only surgical intervention had negative FACT change scores, and those who received a treatment combination of surgery and radiotherapy had a larger positive FACT mean change score. However, patients with small tumors treated with palliative or alternative treatment had the highest positive FACT-HN, FACT-HN (TOI) and FACT-HN (MAQ) mean change score. For moderately-sized tumors (>2–4 cm), a treatment combination of surgery and radiotherapy yielded a high negative FACT mean change score, whereas the surgical intervention resulted in a high positive mean change score. For patients with tumors above moderate size (>4–6 cm), a higher positive FACT-HN (TOI) mean change score was noted among those treated with a combination therapy than those treated with surgical, radiotherapy and palliative care or alternative treatment (which recorded a negative mean change score). By contrast, there was a negative FACT-HN (MAQ) mean change score noted for surgery, radiotherapy and a combination of both treatments for this tumor size.

In terms of patients' FACT-HNSI head and neck symptom index mean change score, patients with small tumors receiving palliative care or alternative treatment had the highest positive change scores whereas surgical interventions yielded negative mean score changes. However, the opposite pattern was noted among patients with moderately-sized tumors, whereby those who were surgically treated had a higher positive FACT-HNSI mean change score than those receiving palliative or alternative care and combination therapy. For tumors above moderate size, radiotherapy resulted in slightly higher positive FACT-HNSI mean change than the combination therapy and surgical intervention (negative FACT-HNSI mean change score). Patients with larger tumors who underwent surgical treatment reported a slightly higher negative FACT-HNSI mean change than those receiving radiotherapy.

## Discussion

This 3-month longitudinal study involved a cohort of 42 oral cancer patients who were interviewed through 3 time points; before treatment, and then 1 and 3 months after commencing treatment. Overall, HRQoL of patients became worse than baseline during first follow-up, which then improved by the second follow-up. At 3 months follow-up, patients receiving surgical interventions reported better HRQoL than those undergoing other types of treatment modality.

Overall, the pre-treatment HRQoL scores for this cohort were in the third quartile range of possible scores. The same was also observed with all pre-treatment subscale scores. Patients' physical and social well-being scores were at the upper end of the third quartile range whereas their functional scores were at the lower end of this range. This indicated that, the HRQoL of patients at diagnosis (pre-treatment) was generally above average; that is, patients were able to perform their normal day-to-day activities in spite of having some symptoms. This finding is comparable to that from other studies, although pre-treatment FACT-G and head and neck scores were somewhat higher in earlier studies (20,21).

The drop in FACT summary scores at 1-month after commencing treatment was reflected by significant deterioration in scores in the physical, functional and head and neck subscales. Surprisingly, patients' symptom index scores [FACT-HNSI and FACT-HNSI (MAQ)] reduced only very slightly despite anticipated post-treatment symptom-effects, such as, trismus, limitation of shoulder movement, and difficulty in chewing, speech and swallowing. In contrast, patients' emotional well-being improved and there was hardly any change in their social well-being from pre-treatment. Family support and good coping skills could be plausible reasons for this. These findings are consistent with earlier studies on patients with cancer of the oral cavity, oropharyx or larynx (21-23).

At 3-month after commencing treatment, patients' summary scores generally improved, although not all returned to pre-treatment levels [FACT-HN, FACT-HN (TOI), FACT-HN (MAQ)]. Overall, there was only

**Table 3** Factors associated with patients' HRQoL change (FACT mean change score) at second follow-up

| HRQoL outcome | Interaction between factors | df | F | P value | Partial eta squared | Observed power |
|---|---|---|---|---|---|---|
| FACT-HN | Tumor size * treatment type | 5 | 3.152 | 0.022 | 0.352 | 0.808 |
| FACT-HN (TOI) | Tumor size * treatment type | 5 | 2.618 | 0.045 | 0.311 | 0.720 |
| FACT-HNSI | Tumor size * treatment type | 5 | 2.707 | 0.040 | 0.318 | 0.736 |
| FACT-HN (MAQ) | Tumor size * treatment type | 5 | 3.226 | 0.019 | 0.357 | 0.819 |

The asterisk * is to denote the interaction between tumor size and treatment type. HRQoL, health-related quality of life; df, degree of freedom; MAQ, Malaysian added questions.

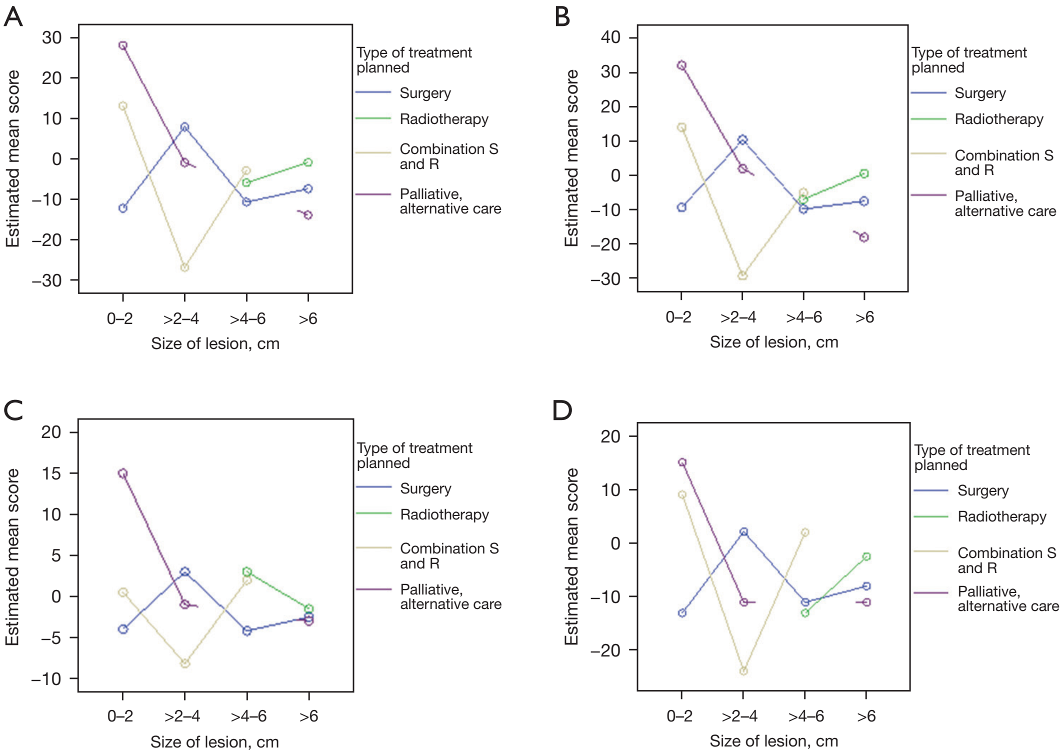

**Figure 4** Interaction between tumour size and treatment type with FACT mean score change from baseline to second follow-up for (A) FACT-HN, (B) FACT-HN (TOI), (C) FACT-HNSI, and (D) FACT-HN (MAQ). S, surgery; R, radiotherapy.

a slight improvement in patients' symptom index scores at this point. The gradual physical, head and neck and functional recovery concurs with the assertion that these three domains constitute a major aspect of life quality in the first year after intra-oral surgery (24). Despite patients' immediate physical and functional deterioration in the month following treatment, their emotional well-being continued to improve from baseline to 3-month post-treatment, resulting in significant difference in emotional subscale scores between pre-treatment and second follow-up visit. This finding concurs with those of other studies (22,23) and supports the fact that, patients tend to undergo psychological adjustments to their condition and improve their manner of coping which appear to negate the influence of physical and functional deterioration on their emotional well-being (24,25). Moreover, the joint family system practiced across all ethnicities in Malaysia (whereby the patient would be living with their family members) would have facilitated better family support in order for them to emotionally and socially cope with the impact of their illness. As such, it would be desirable to gain more insight into the role of coping, resilience and psychological adaptation through future prospective studies.

The proportion of patients with 'poor' and 'very poor' self-rated HRQoL almost doubled from baseline to 1-month but fell below baseline levels at the 3-month follow-up. There was a larger proportion of patients with an 'average', 'good' or 'very good' HRQoL at baseline, which then shifted towards a larger proportion of patients rating themselves in the very poor, poor or average HRQoL categories 1-month after commencing treatment. However, by third month of commencing treatment, this distribution had returned almost to that seen at baseline. This pattern conforms to the general patterns seen with the FACT summary scores and most of the subscale scores, indicating the usefulness and validity of the global response question as a reasonable reflection of patients' HRQoL. Although Cella (26) argued against selecting global response questions as a primary outcome in clinical trials (especially in the absence of a control group), the findings of the current study may lend some weight to the argument of Hobday (27) that the global response question is a good reflection of patients' overall HRQoL because it is able to synthesize all aspects of HRQoL into a single outcome.

Patients who underwent surgical intervention experienced first a decline in HRQoL by the first month after operation, followed by an improvement either to, almost to or more than their baseline HRQoL levels by the third month after treatment. These findings are consistent with earlier studies of patients with squamous cell carcinoma who experienced improvement in HRQoL in the third month (28-30). In contrast, patients who underwent other treatment modalities (namely, radiotherapy, a combination of palliative and alternative care) experienced a progressive decline in their HRQoL from baseline to second follow-up. At 3 months after commencing treatment, the HRQoL of patients who had undergone surgery and other treatment modalities differed significantly, and this difference from baseline to the second follow-up was consistently noted for all of the FACT summary scores, which mirrored patients' physical and functional well-being at this time point. In contrast, the social well-being of both patient groups changed very little, whereas the emotional well-being of patients who had undergone surgery appeared slightly better than the 'other treatment' group, although this difference was not significant. These findings differ from those of another prospective study with oral cancer patients (29) which indicated that, no significant differences were detected after 1 year between patients who were surgically treated and those who received neoadjuvant treatment. Moreover, it has been reported previously that emotional well-being is impacted differently according to patient age groups (31). It is also noteworthy that the set of Malaysian questions teased out significant differences in HRQoL between patients undergoing both treatment modalities at 3-month after commencing treatment. Notably, patients' symptom-related burden became progressively less as they recovered from their surgery. In contrast, those who received other treatment modalities (which are less invasive in nature) may have experienced symptom alleviation initially which could not be sustained until second follow-up. Likewise, other study findings resonate that a combination treatment modality of either post-operative radiotherapy and surgery, or adjuvant chemotherapy significantly reduces HRQoL, in comparison to surgery alone (22,28,29,32-34). Presumably because most patients who are indicated for other treatment modalities more often than not are those with more advanced stages of cancer (35,36), it would be not surprising to see those patients regress in their HRQoL over time. Moreover, surgical interventions normally are completed at one sitting followed by a definite period of patient recovery, in contrast to radiotherapy/combination therapy, which are done in cycles. At first follow-up, patients undergoing radio/chemo or combination therapy would have been in the midst of their treatment, thus explaining the decline in their HRQoL after which these cycles may have been continued, resulting in further deterioration of their QoL in the second follow-up. In contrast, those undergoing surgical intervention only, experienced the decline only at first follow-up due to post surgery effects, which they recovered from by the second follow-up, thus improving their HRQoL. These findings suggest that surgical intervention favors an improvement in patients' overall HRQoL (at 1- and 3-month after commencing treatment) over other treatment modalities. This is reflected in patients improved physical, functional, emotional well-being and head and neck concerns. Thus, it would be fitting that further research is done on the impact of the different treatment modalities with larger sample sizes, in order to be able to study the HRQoL effects of each treatment modality in greater detail.

An interaction between tumor size and type of treatment was found to be associated with the observed FACT mean change scores 3-month after commencing treatment; namely, the FACT-HN, FACT-HN (TOI), FACT-HN (MAQ) and FACT-HNSI symptom index. These findings suggest that, in patients with larger-sized tumors (>6 cm), radiotherapy yielded less HRQoL deterioration, followed by surgical intervention and palliative care/alternative care. However, patients with smaller-sized tumors (>2–4 cm) experienced marked improvement in HRQoL with surgical intervention. In contrast, those receiving palliative or alternative care, and combination treatment (of surgery and radiotherapy) experienced the largest declines in HRQoL at 3-month. In patients with the smallest sized tumors (0–2 cm), very notable improvement in HRQoL was observed with palliative care or alternative treatment and a combination treatment, whereas surgical intervention caused a decline in HRQoL at 3-month. Differences in patients' FACT mean score changes were most obvious for those with smaller-sized tumors who received different types of treatment. These patterns were consistent for the abovementioned FACT summary scores and support the assertion that treatment-related factors do influence HRQoL after treatment (25,34,37). Although limited by small sample size, the current study's findings indicate that patients with tumors of different sizes respond differently in their HRQoL change with different types of treatment. Further longitudinal research with an adequate sample size for each type of treatment modality would help shed greater light on the interaction between these clinical factors in association with patients' HRQoL change after treatment.

Cancer survivorship is a very challenging period, due to the consequence of complex treatment process and its residual side effects that could significantly impact physical, psychological, sexual, social and functional well-being throughout the post-treatment phase. Following treatment of their disease, there are potentially various issues or concerns that the patients will face that could significantly impact their HRQoL. Findings of this study clearly shows that there are unmet needs and HRQoL concerns of the patients during the first 3 months. As such, it is imperative that these needs be identified and addressed within the first few months upon commencement of treatment. One such intervention could be the Patient Concerns Inventory (PCI), an aid to facilitate patients to identify issues or concerns that they want to discuss during their follow-up consultations (38). A study conducted among Malaysian oral cancer patients using the PCI identified that patients were most concerned with their physical status, emotional status and personal functioning (39). For physical status, the concerns most frequently raised were in relation to chewing, pain in the area of head and neck, salivation and limited mouth opening, which is a reflection of impact of treatment. In terms of emotional status, anger, frustration, anxiety and fear of recurrence were the most reported concern, whereas for personal functioning, sleep disturbance was of greatest concern. Although social/family relationship issues were the least selected concern, it does not necessarily mean the issue is not of relevance to this population. Instead, it is plausible to assume that patients consider these issues not appropriate/relevant to be discussed with their specialists, or they may feel intimidated to ask their clinicians/specialists too many questions. This highlights the need for supportive care for oral cancer patients in Malaysia, which is currently lacking. Moreover, in a more recent study (40), the PCI was shown to be able to discern between different levels of post-treatment psychological distress and HRQoL concerns.

The limitations of this study should be addressed. First, the sample size for the longitudinal study was less than ideal. Despite involving seven hospital-based oral specialist clinics, only 76 patients were recruited at baseline as this was solely dependent on the number of new oral cancer cases seen at these clinics. Second limitation is the high attrition rate with an average of 22%, (20% at 1-month and 25% at 3-month) which rendered the final cohort size to be small. The high attrition rate was due to patients refusing to continue treatment, being uncontactable, having died, being too ill to attend follow-ups or receiving follow up treatment modalities (such as radiotherapy) at hospitals in different districts. In terms of patients' clinical details, it was observed that there were some clinical differences between patients at baseline with patients at follow-up stages. For example, more patients with larger tumors and advanced stage tumors at baseline dropped out at subsequent follow-ups. In addition, the proportion of patients undergoing radiotherapy decreased from baseline to the follow-up stages as did those who were undergoing palliative or alternative care. Presumably, high attrition among these group of patients is primarily due to their frail and debilitated condition following their treatment and tumor size. Third, interviewer bias is a systematic alteration concerning how information is sought, noted or interpreted (41,42). As the majority of patients involved in this study lacked formal education, face-to-face interviews were adopted as the mode of administration of the questionnaires. This is to avoid significant negative impact to the data collection process such as questionnaires returned without being completely filled. However, this bias was minimized by the process of training and standardization of data collectors prior to data collection. Fourth, the use of patient proxies as intermediaries could have been another source of bias in this study. The need to obtain vital information from patient proxies at post-operation had to be weighed against not getting any information at all especially in circumstances whereby some elderly patients had difficulty speaking and were still very ill and frail. However, considering that most patient proxies were family members, their input was deemed vital. Moreover, previous studies on patient-partner agreement have reported proxy assessment to be a collaborative and valuable alternative source (43). Fifth, some heterogeneity in the patient cohort exists in terms of their disease status at diagnosis and their treatment status at the 3 months follow-up. Nevertheless, the purpose of this paper is to give an overview of a cohort of oral cancer patients' HRQoL impacts before and after undergoing different treatment modalities over a 3-month period.

## Conclusions

Surgical intervention favored an improvement in patients' overall HRQoL over the other treatment modalities at 3-month after commencing treatment. Notably, an interaction between tumour size and treatment type was associated with HRQoL change during this time trajectory. These findings can be generalised to oral cancer patients in Malaysia taking into account the study limitations. Further studies using larger samples would help gain a deeper insight into how each treatment modality impacts oral cancer patients' HRQoL.

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