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Hao-Wei Tang

Tung-Hao Chang

Kuan-Lin Chen

Kuo-Yang Tsai

Su-Fen Liao

See next page for additional authors

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Original Article

Evaluation of Clinical Morbidities and Their Influence on Quality of Life in Patients with Oral Cavity Cancer after Radiotherapy

Hao-Wei Tang[1*], Tung-Hao Chang[2,3*], Kuan-Lin Chen[4], Kuo-Yang Tsai[5], Su-Fen Liao[4,6,7], Wei-Te Wang[4]

[1]Department of Physical Medicine and Rehabilitation, Hongren Hospital, Yuanlin City, Changhua County
[2]Department of Radiation Oncology, Changhua Christian Hospital, Changhua
[3]Department of Radiology, Yuanpei University of Science and Technology, Hsinchu
[4]Department of Physical Medicine and Rehabilitation, Changhua Christian Hospital
[5]Department of Oral and Maxillofacial Surgery, Changhua Christian Hospital
[6]Division of Pediatric Rehabilitation, Changhua Christian Children's Hospital
[7]Department of Physical Therapy, Hung Kuang University, Taichung
([*]Co-first authors)

Background: Oral cavity cancer is the most common cancer in middle-aged men in Taiwan. Radiation fibrosis syndrome and lymphedema are the leading side effects in patients with oral cavity cancer, and can deteriorate their quality of life (QOL). The aim of this study was to prospectively evaluate common morbidities and their influences on QOL in patients with oral cavity cancer.

Methods: 27 patients with oral cavity cancer who received surgery and radiotherapy (RT) were recruited. Clinical evaluations of each patient included the VAS pain scale, the lymphedema scale, facial distance measurement for lymphedema, maximal interincisal distance (MID), range of motion (ROM) of the neck and shoulder, Constant shoulder score, and the EORTC QLQ (QLQ C30, H-N35) shortly after RT, and at 3 months and 6 months after RT.

Results: ROM of the neck and shoulder, and the Constant shoulder score were the worst shortly after RT. The participants had moderately decreased neck ROM, and a deficit in abduction, internal/external rotation of the shoulder and the Constant score, even 6 months after RT. Lymphedema was detected in all patients. The VAS pain score (4.8±2.1) was the worst shortly after RT, and was correlated with the lymphedema scales ($p < 0.001$), the Constant score (Rt- $p = 0.003$, Lt- $p=0.02$) and MID($p = 0.049$). In terms of QOL, fatigue, insomnia, financial difficulties, dry mouth, mouth opening and sticky saliva were the predominant morbidities, and showed no significant improvement.

Conclusions: Dry mouth, impaired mouth opening, sticky saliva, insomnia and lymphedema were the major long-term morbidities in patients with oral cavity cancer after radiotherapy. Improvement of neck ROM and shoulder abduction in patients who have undergone extensive neck dissection should be given more clinical attention. (Tw J Phys Med Rehabil 2020; 48(1): 1 - 13)

Key Words: oral cavity cancer, lymphedema, quality of life, rehabilitation, radiation fibrosis syndrome

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Correspondence to: Dr. Su-Fen Liao, Department of Physical Medicine and Rehabilitation, Changhua Christian Hospital, No. 135, Nanxiao Street, Changhua County 500, Taiwan
Tel：(04) 7238595 ext. 7439 E-mail：sueliao3@gmail.com
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INTRODUCTION

Head and neck cancer (HNC) is a common cancer, and the lip and oral cancer is the sixteenth diagnosed cancer worldwide.[1] Incidence of HNC is strongly associated with certain lifestyle risk factors like tobacco and alcohol consumption, and 66% of HNC are diagnosed at advanced stages (III or IV).[2,3] The effective curative treatment for HNC is surgery, radiation therapy (RT) and/or chemotherapy in different combinations.[4] Extensive neck dissection is a standard operation in patients with advanced oral cancer and tongue cancer. However, the presence of pain and deterioration of shoulder and neck function after neck dissection are extreme considerable problems in patients.[5-7] Speksnijder CM et al reported that neck dissection and extensive reconstruction are related to deterioration of shoulder function especially active shoulder abduction.[5] And he also found that impaired lateral flexion of the neck and pain during neck movement in oral cancer patients who received extensive neck dissection even one year after surgery.[5] Pain of HNC patients is the result of multiple generators, including tissue destruction by invasive tumors (or metastases), inflammatory and neuropathic pain, paraneoplastic neuropathic syndromes, and pain from cancer management (surgery, chemotherapy, and radiotherapy).[8] Pain is common in HNC patients with an incidence of 49.5% prior to cancer therapy, 81% during the therapy, 70% at the end therapy, and still 36% 6 months after treatment.[9] Cramer JD concluded that pain remains a significant problem in HNC and is associated with worse quality of life(QOL).[10]

Surgery and RT can disrupt the lymphatic structure and functions, consequently patients with HNC may be at high risk for developing the secondary lymphedema.[11,12]

Lymphedema is a common late effect in patients with HNC, which develops in multiple external and internal anatomical locations.[11,12] Existing evidence indicated that 12~75% patients with HNC developed secondary lymphedema.[13-16] Chronic lymphedema accompanied with post-radiation fibrosis induced trismus that may result in long-term cosmetic, functional, and psychosocial consequences.[4,12,17] Furthermore, lymphedema presence leads to decrease range of motion (ROM), impaired swallowing, neck fibrosis and pain.[12,16]

All these morbidities in patients disturb their QOL, cause negative body image and social isolation.[18-21] The incidence of oral cancer is the most common cancer in Taiwanese middle-aged men,[22] and many of these patients are suffering from morbidities.[18-21]

The endpoint of clinical research is not only on survival but also on patients' experience and QOL outcome.[4] In this study, we evaluated the progression of common morbidities and their influence on QOL in patients with oral cancer after receiving surgery and RT.

MATERIALS AND METHODS

This is a prospective observation study on oral cancer patients, conducted at a medical center, Changhua Christian Hospital, Taiwan. This study was approved and ethical clearance was obtained from the hospital Institutional Review Board (IRB 120506). All participants provided written informed consent forms for the participation.

For this study, a total of 27 patients (26 males and 1 female) with different stages of oral cavity cancer were enrolled. All patients received surgery and RT treatments between Oct, 2012 and Sep, 2014; they did not receive regular rehabilitation program in study period. Patients with recurrence of cancer, injured shoulder or neck with ROM of shoulder less than 120 degree or ROM of neck less than 50 degree were excluded.

Demographic data including gender, age, body mass index (BMI), staging of cancer, surgical method, the number of removed lymph nodes, and dose of RT were obtained from the participants' medical records. Participants were underwent evaluation when they were shortly after RT, 3-month and 6-month after RT. Clinical measures, including visual analog pain scale (VAS), ROM of neck (forward flexion, extension, rotation and lateral flexion) and shoulder (flexion, extension, abduction, internal rotation and external rotation), Constant shoulder score, maximal interincisal distance (MID), Földi and Miller lymphedema scale were assessed. Földi scale[23] separated lymphedema as stage 0,1,2 and 3; Miller scale [24] graded lymphedema from 0 to 4 depending on the severity; both of them were used to assess the clinical stage of lymphedema. The objective measurement of

lymphedema was evaluated by ultrasonography (US) and face distance measurement. The skin to bone distance (SBD) at seven locations in the face and neck (zygomatic arch, ascending mandibular ramus, and horizontal mandible of both sides; and hyoid bone)was recorded by US.[25] For tape measurements, seven anatomic marks including tragus, mental protuberance, mouth angle, mandibular angle, nasal wing, internal eye corner, and external eye corner were chosen as the reference points; a sum of each side seven distances were calculated as Piso[26] used to evaluate head-neck edema. The US measurement was performed by using a device (Siemens, Acuson Antares PE) with a 10-13MHz linear scanner.

Passive ROM of neck and shoulder were measured using goniometry in sitting position.[27] The shoulder function was assessed using Constant shoulder scale,[28] which could reliably assess shoulder impairment in cancer patients after neck dissections.[29] The test included symptom scores (pain, sleep, recreation, and vocational activities), ROM, and shoulder strength. Scoring range from 0-100 with higher scores indicated better shoulder function.

The quality of life was assessed by European Organization for Research and Treatment of Cancer (EORTC QLQ C30 and H&N35 (head and neck model)) Chinese Taiwanese version, which has been used in numerous studies to evaluate the QOL of cancer patients and the combination of these surveys gives the ability to identify disease-specific side effects.[19,30] The EORTC was evaluated before RT, shortly after RT, 3- and 6-month after RT.

Statistical analysis

Descriptive statistics were used for demographic variables. The data were provided as mean ± standard deviations (SD). The differences of VAS pain score, ROM, MID, lymphedema scale, face distance, US measurement and EORTC QOL scores between each evaluation were analyzed using generalized estimating equations (GEE). The Pearson Correlation was used to analyze the correlation between the variables and VAS scores. p values of <0.05 were considered statistically significant. All analyses were conducted with SPSS for Windows, Versions 18.

Table 1. Demographic and Clinical characteristics of study participants

Variables	*n* (%)	Mean (SD)
Age	27	56.7(10.3)
Sex		
Female	1(4)	
Male	26(96)	
BMI (kg/m^2)		21.2(3.1)
Stage		
I	3(11)	
II	2(7)	
III	1(4)	
IVa	21(78)	
Surgery method		
RND	1(4)	
mRND	11(41)	
FND	5(18)	
SND	4(15)	
Bilateral ND	6(22)	
Preserved Spinal accessory nerve	20(74)	
Removed lymph nodes		39.8(16.4)
Radiation	27(100)	
Dose (cGy)		6530(272)
Friction		32.6(1.4)
Chemotherapy (C/T)		
Nil	6(22)	
CCRT	19(70)	
Neoadjuvant C/T	1(4)	
Oral C/T	1(4)	

RND= radical neck dissection;
mRND= modified radical neck dissection;
FND= functional or neck dissection;
SND= selective neck dissection;
ND= neck dissection;
CCRT= concurrent chemoradiotherapy;
C/T= Chemotherapy.

Table 2. Changes in range of motion of neck

Variables(normal value°)	Shortly after RT(SD)	3-month after RT(SD)	6-month after RT(SD)
n	27	16	11
Forward flexion(60)	32.8(6.9)* †	38.3(6.8)* ‡	41 (7.9) †‡
Extension(75)	34.6(8.8) *	40.7(7.8) *	40.7(8.1)
Rotation(80)			
Right	31.1(9) *†	37.1(9.5)*	36.5(8.3)†
Left	32.3(10) *†	38.4(10.8)*	36.9(10) †
Lat flexion(45)			
Right	23.5(8.4) *†	24.2(5.7) *‡	25.8(6.2)†‡
Left	20.9(8.8) *†	21.5(5.7) *‡	25.3(7)†‡

RT= radiation therapy; Lat=lateral. In Generalized Linear Models analysis:

*p< 0.05 the data of shortly after RT compared with that of 3-month after RT

† p< 0.05 the data of shortly after RT compared with that of 6-month after RT

‡ p< 0.05 the data of 3-month after RT compared with that of 6-month after RT

Table 3. Changes in range of motion of shoulder

Variables(normal value°)	Shortly after RT(SD)	3-month after RT(SD)	6-month after RT(SD)
n	27	16	11
Right shoulder			
Flexion (180)	172.7(8.6) †	175.3(8.1)	175.5 (8.3) †
Extension (60)	54(25.8)	50.3(5.6) ‡	53.2(8.4)‡
Abduction (180)	162.8(16.1) *	169.4(13.4) *	166.8(16.5)
Internal rotation (70)	51.6(14.3)	52.4(16)‡	52.3(16.2)‡
External rotation (90)	60(14.9)	57.4(17.7)‡	59.4(20.1)‡
Left shoulder			
Flexion (180)	171.6(16.1)	172.2(10.8)	172.3 (10.3)
Extension (60)	53(6.1) *†	56(5.4)*	57.8(6.2) †
Abduction (180)	163.2(22.5) *†	168.4(15.2) *	169.5(13.1) †
Internal rotation (70)	50.5(14.7) †	52.3(18.2)‡	52.8(14.5)†‡
External rotation (90)	61.1(16.9) †	64.5(16.7)	65.7(14.8)†

RT= radiation therapy. In Generalized Linear Models analysis:

*p< 0.05 the data of shortly after RT compared with that of 3-month after RT

† p< 0.05 the data of shortly after RT compared with that of 6-month after RT

‡ p< 0.05 the data of 3-month after RT compared with that of 6-month after RT

Table 4. Measurement of Pain, Lymphedema and Constant shoulder score

Variables	Shortly after RT(SD)	3-month after RT(SD)	6-month after RT(SD)
n	27	16	11
VAS	4.8(2.1)* †	1.7(1.0)* ‡	0.9 (1.1) †‡
MID (cm)	4.8(1) *†	5.4(0.7) *	5.6(0.8) †
Föeldi scale	2.7(0.8) *†	1.7(0.8)*	1.5(0.7)†
Miller grade	2.4(0.8)*†	1.1(0.3)*	1.1(0.3) †
SBD-Hyoid bone (mm)	12.5(3)	12.5(3.1) ‡	11.8(3.7)‡
SBD-Left horizontal mandible (mm)	13(3.8) *	14.6(3.5) *	13.8(3.6)
Facial distances (cm)			
Right	80.5(4.7)	81.8(4.6)	80.9(5.5)
Left	78.6(5.7)	79.3(5.6)	81.1(4.2)
Constant shoulder score			
Right	67.4(8.2) *†	74.1(9.4) *	78.5(6) †
Left	71.3(9.1) *†	78.1(7.1) *	79.9(5.4) †

RT= radiation therapy ; VAS= visual analog pain scale; MID= maximal interincisal distance; SBD= skin to bone distance.In Generalized Linear Models analysis:

*p< 0.05 the data of shortly after RT compared with that of 3-month after RT

†p< 0.05 the data of shortly after RT compared with that of 6-month after RT

‡p< 0.05 the data of 3-month after RT compared with that of 6-month after RT

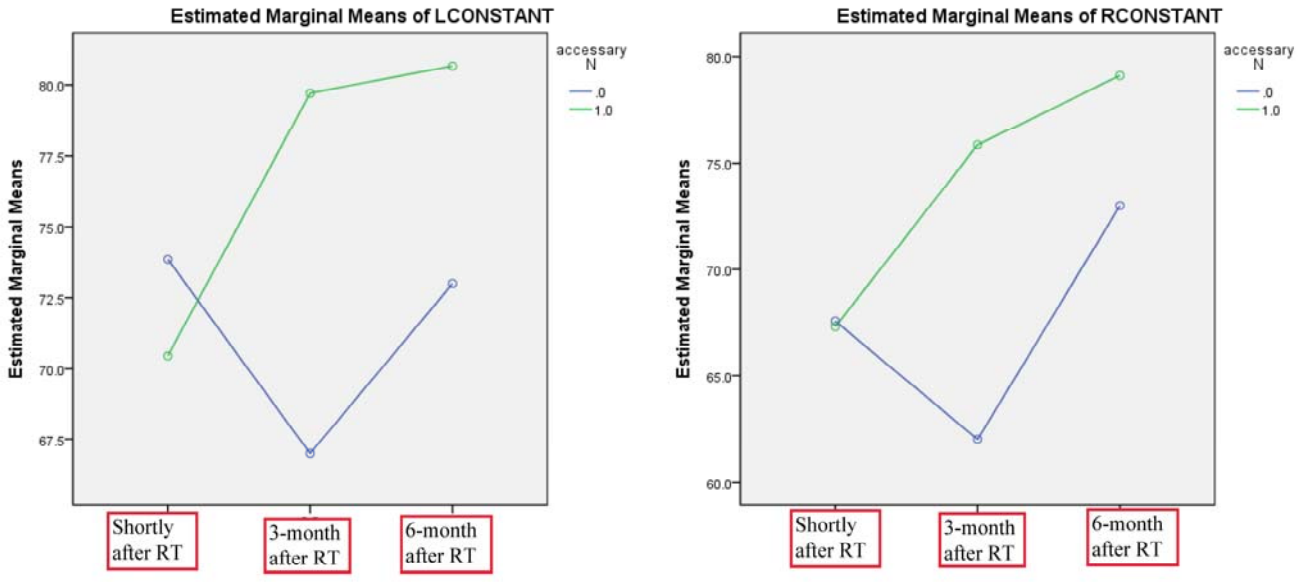

Figure 1.

Preserved spinal accessory nerve (SAN) had better Constant shoulder score at 3- and 6-month after RT , but the significant difference was only noted in Lt Constant shoulder score (p=0.049). 0- sacrificed spinal accessory nerve; 1- preserved spinal accessory nerve

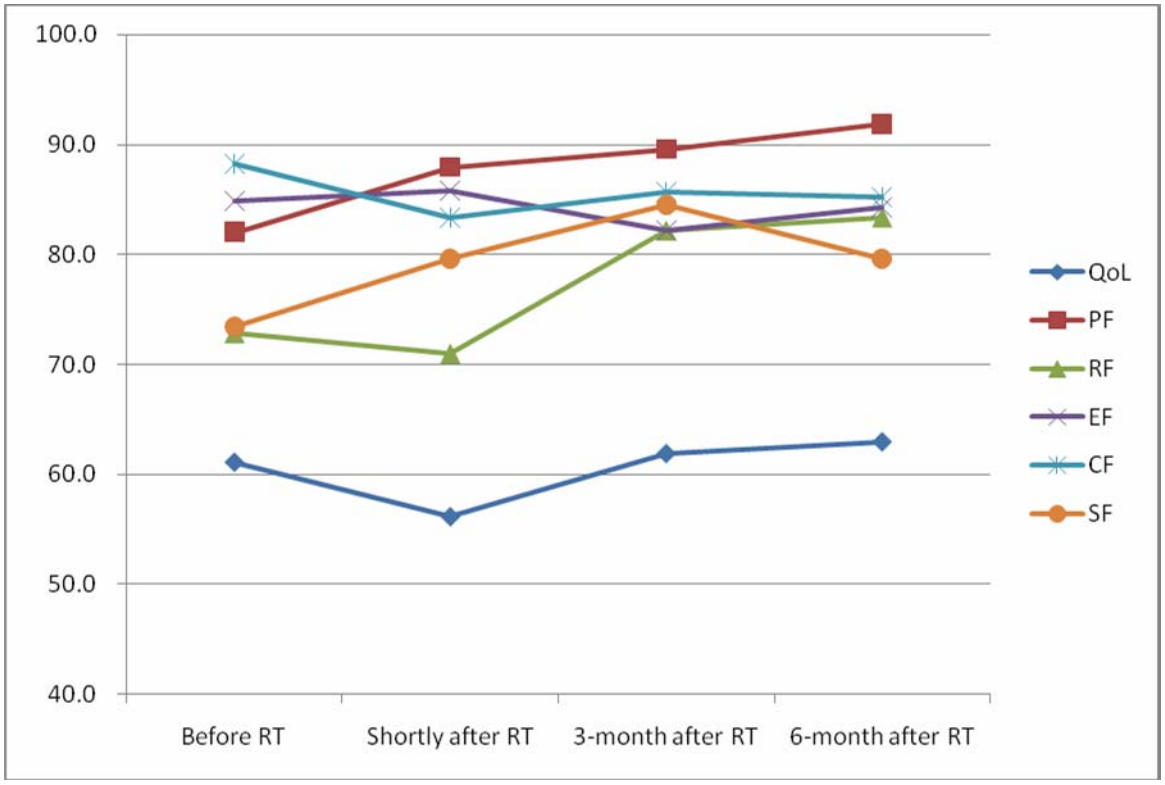

Figure 2. The EORTC QLQ-C30 general health and functional scales
QoL= global health status; PF= physical functioning; RF= role functioning; EF= emotional functioning; CF= cognitive functioning; SF= social functioning.

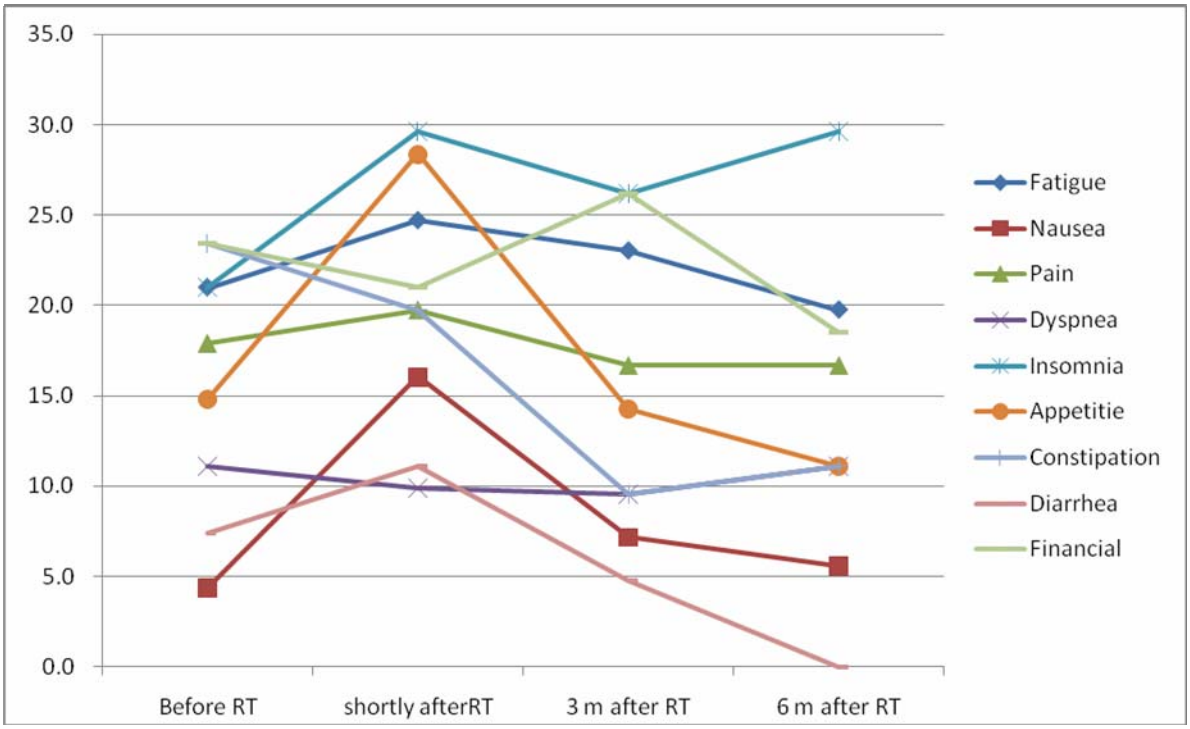

Figure 3. The symptom scales of EORTC QLQ C-30.

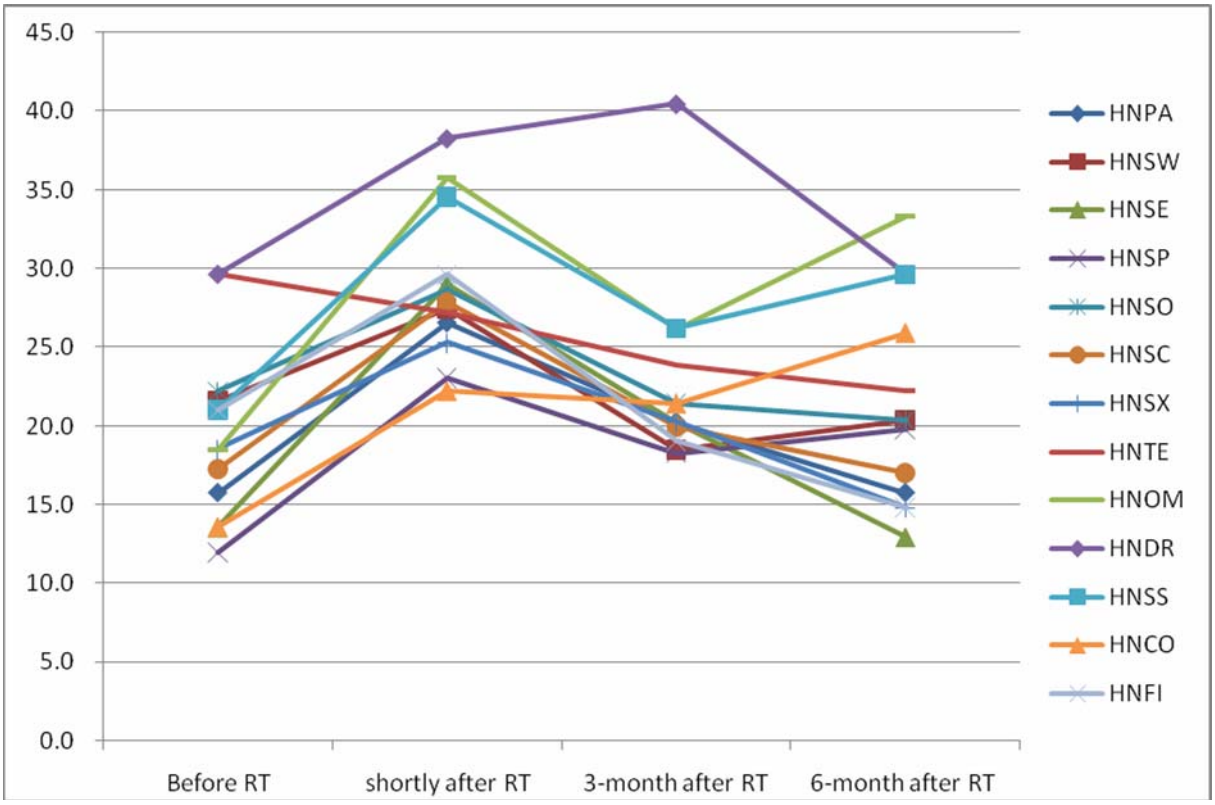

Figure 4. The symptom scales of EORTC QLQ-HN 35
HNPA= Pain; HNSW= swallowing; HNSE= senses problems; HNSP= speech problems; HNSO= trouble with social eating; HNSC= trouble with social contact; HNSX= less sexuality; HNTE= teeth; HNOM= opening mouth; HNDR= dry mouth; HNSS= sticky saliva; HNCO= coughing; HNFI= felt ill.

RESULTS

Out of 27 patients, 16 patients completed 2nd follow-up (3-month after RT), and 11 patients completed 3rd follow-up (6-month after RT). The mean age of patients was 56.7±10.3 years, and their BMI was 21.2±3.1 kg/m^2 (Table 1). Among 27 patients, 21 patients (78%) were identified as advanced stage of oral cavity cancer (stage IVa). Most patients (67%) required extensive surgery and only 33% patients received limited surgery (functional or selective neck dissection, SND). The number of removed lymph nodes was 39.8±16.4. All patients received RT at the radiation dose of 6530±272 cGy and 70% patients received concurrent chemoradiotherapy (CCRT) (Table 1).

Changes in ROM of neck and shoulder

The degree of ROM for neck and shoulder of patients were measured shortly after RT, 3-month and 6-month after RT, and compared with respective normal values. The ROM of neck forward flexion, extension, rotation and lateral flexion were the worst shortly after RT, and these variables were significantly ($p< 0.05$) improved 3-month after RT. The improvement of neck forward flexion and lateral flexion were further continued until 6-month after RT (Table 2). But the median neck movements were in the range of 25.3 to 41 degrees (normal range of neck, 45–80°), decreased 50% when compared with normal range.

The impaired abduction of right shoulder and extension and abduction of left shoulder shortly after RT were significantly improved 3 months later. The flexion of right shoulder, and all ROM variables of left shoulder (except flexion) were notably improved 6-month after RT when compared with shortly after RT. Furthermore, the

extension, internal rotation and external rotation of right shoulder, and internal rotation of left shoulder at 6-month after RT were significantly better than that of 3-month after RT in patients (Table 3). The median shoulder movements were in the range of 52.3 to 175.5 degrees (normal range, 60–180°),[27] and the range of shoulder flexion was near full range, 10-15 degree deficit in shoulder abduction and 15-25 degree deficit in internal/external rotation at 6-month after RT.

Changes in pain, lymphedema and Constant shoulder score

The Constant shoulder score was the worst shortly after RT, and significantly improved 3 months later. But there was no difference between the scores of 3- and 6-month after RT (Table 4). The patients who were preserved spinal accessory nerve (SAN) had better Constant shoulder score than the patients who were sacrificed SAN in 3- and 6-month after RT, but the significant difference was only noted in Lt Constant shoulder score (p=0.049) in GEE analysis (Figure 1).

In the lymphedema evaluation, Foldi scale and Miller score were the worst shortly after RT, and significantly improved 3 months later. But there was no difference between the scales of 3- and 6-month after RT (Table 4). The SBD on hyoid bone of 6-month after RT was better than that of 3-month after RT, and SBD on left horizontal mandible bone of 3-month after RT was better than that shortly after RT. But there was no difference of other results in US and tape measurements. In trismus, the MID were the worst shortly after RT, and significantly improved 3 months later. But there was no difference between the MID of 3- and 6-month after RT (Table 4).

The VAS pain score (4.8±2.1) were the worst shortly after RT. Although the mean pain severity was mild cancer pain[31], but moderate and severe pain were noted in more than half patients [31]. The pain score significantly improved 3 months (1.7±1.0) later and continued improving 6-month after RT (0.9±1.1). There was significant correlation in pain with lymphedema scales (p<0.001), Constant shoulder score (Rt- p=0.003, Lt-p= 0.02) and MID (p=0.049). We also found the pain was not correlated with most items of QOL, it was only correlated with diarrhea (p=0.001) in QLQ-C30 and pain (p= 0.047) and social eating (p= 0.005) in QLQ-HN35.

Changes in QOL

All EORTC scales and single items were scored and linearly transformed scales of 1 to 100. The EORTC QLQ-C30 general health and functional scales were depicted in Figure 2 and the higher scores revealed better function. In functional scales and global health status, only social function (p=0.02) showed difference between before RT and 3-month after RT (Figure 2). For the symptom scales of QLQ C-30, higher scores indicate greater impairment. The nausea and appetite were the poorest when finished RT, and significantly improved 3-month after RT. The diarrhea improved much at 6-month after RT. The constipation was noted before RT, and improved at 3-month after RT. The fatigue, pain, insomnia and financial difficulties were the worst scores in QLQ-C30, and did not improve during the follow-up even 6-month after RT (Figure 3). The difference of more than 10 points on the EORTC subscales were considered clinically significant,[14] which was the case in our study.

The disease-specific QOL was assessed by EORTC QLQ-HN 35 (Figure 4). For the scales of QLQ HN 35, higher scores mean greater impairment. Dry mouth, impaired mouth opening and sticky saliva were the most predominant problems in our patients, and did not improve in the end of follow-up. The pain, speech, impaired mouth opening and sticky saliva were significantly progressed compared before RT with shortly after RT, and did not show any improvement in follow-up. The senses and social contact were the poorest shortly after RT and improved at 6-month after RT.

DISCUSSION

In our study, the ROM of neck were the worst shortly after RT, and gradually improved. But the neck movements decreased 50% when compared with normal range even 6-month after RT. This suggests that most of the participants had moderately decreased neck ROM even 6-month after RT. It is grade 2 late radiation morbidity defined by Radiation Therapy Oncology Group (RTOG) criteria.[32] In contrast, Deng J et al.[33] reported that most of participants 3 months or more after HNC treatment had mildly to moderately decreased neck ROM in six directions. Our patients had more restricted neck

ROM because most of them were advanced oral cancer, more extensive surgery, and applied RT in all participants. As a 1-year prospective cohort study of 145 oral cancer patients performed by Speksnijder CM, reported more extended neck dissection induced greater deterioration in neck function and also found the patients treated with bilateral neck dissection still showed impaired lateral flexion of the neck in one year after intervention.[5] As above finding, we should extend the period of regular rehabilitation follow-up in patients with advanced oral cancer to 1 year after RT.

As the ROM of neck, the ROM of shoulder was the worst shortly after RT, and gradually improved. Although range of shoulder flexion is near full range, there were deficits at shoulder abduction, internal and external rotation in the end of follow-up. The limitation of shoulder movement was as grade 1-2 late radiation morbidity in joint by RTOG criteria[32]. This is compatible with Speksnijder's conclusion that maximal forward flexion of the shoulder returned to the level of healthy controls and significantly lower maximal abduction of the shoulder than controls at 1 year after intervention.[5] In maximal shoulder abduction, trapezius muscle activity is needed to upward rotate and stabilize the scapula, whereas in maximal forward flexion this upward rotation and stabilization is much less important. The extensive neck dissection will disturb the nerve function of SAN and lead to loss of function of the trapezius muscle, even preservation of the SAN.[5,34,35] This is agreed with our result of shoulder function. The Constant shoulder score improved after RT but still 20-25% deficit when compared with control. Chepeha DB reported that patients receiving modified radial neck dissection had significantly worse shoulder function than patients with SND.[29] This is because most our participants received extensive neck dissection and only 15% patients received SND. We also found the group who were preserved SAN had better Constant shoulder score than sacrificed SAN group at 3- and 6-month after RT. As Eickmeyer SM reported that sparing the SAN during neck dissection is associated with significantly less long-term shoulder disability in 5-year survivors of HNC.[36] We could conclude that although neck dissection would disturb short-term shoulder function, but sacrificed SAN would induce more long-term shoulder disability.

Prevalence of trismus after HNC treatment ranges from 5% to 38%, and the criteria varies.[37] A mouth opening of ≤35 mm has been proposed as a functional cut-off point for trismus.[38] The most common cause of oncology-related trismus is radiation-induced fibrosis, while post-surgical scarring may also play a role.[39] Pauli N et al reported the incidence of trismus was 9% pre-treatment and 28% at the one-year follow-up post-treatment, and the highest incidence, 38%, was found at six-month post-treatment.[4] In our study, the MID increased significantly 3 months after radiation, and the mean MID did not reach the criteria of trismus. There were only three patients (11.1%) who met this criteria of trismus just after RT, but improved in follow-up. It might be too few patients to observe the MID change.

Tumor itself, surgical damage, RT, and chemotherapy may disrupt the lymphatic structures, and resulted in lymphedema.[33] Currently, there was no standard criteria and grading system for lymphedema in head and neck cancer, and various tool has been used in previous studies.[16,26,40-42] We chose Foldi's scale, Miller's score, tape and US measurement to assess lymphedema. In our study, lymphedema severity by scoring system was significantly improved after RT, but still persisted in all participants. And only the SBD of hyoid and left mandible bone showed difference in the follow-up. There was no difference of tape measurement in three follow-ups. It showed the face tape measurement is not sensitive to detect localized lymphedema change in patients with HNC. Literatures suggested that the incidence of post treatment lymphedema of head and neck cancer varies from 12% to 75%. [14-16] Deng J et al reported a prevalence of 75.3% of lymphedema in 81 HN cancer patients 3 months or more after treatment.[16] The incidence is lower than our result, because lower proportion of patients who received both surgery and radiation (49.4%). The prolonged facial edema is also associated with poor prognosis in HN cancer patients.[43]

Pain is common in HNC patients, and still 36% at 6-month after treatment.[9] In our study, HNC patient reported mild pain (VAS= 4.8) shortly after RT, but half patients had moderate or severe pain. As Ohrn KE expressed several oral symptoms were noted 1 month after beginning RT,[44] and Epstein JB concluded that pain increases throughout the course of radiation and persists

following treatment.[45] We found the more severe pain was associated with more lymphedema, and negative effect in trismus and shoulder function. In QOL, most items of QOL was not found to be correlated with pain. It could be explained that the shoulder functional outcome is significantly correlated with pain, but this is not reflected in the scores of QOL questionnaires as Schiefke F 's conclusion.[14] And the pain score of our patients improved in the follow up, it was only 0.9 at 6-month after RT. But Cramer JD had different conclusion that pain remains a significant problem and is associated with worse QOL even years after head and neck cancer treatment.[10]

In QOL, global health and functional scales of QLQ-C30 did not change much. Our finding was similar to Schiefke F's[14] and Wan Leung S's[19] results, both of them performed cross-section studies at 2 years later after treatment. The fatigue, pain, insomnia and financial difficulties were the major concerns in HNC patients, not only in our study but also in previous studies.[14,19] The insomnia is still the highest score in whole study period, cognitive behavior training and some medication could be helpful. The nausea and appetite were the worst just finished RT, then gradually improved as the course of mucositis. The oral mucositis can peak near the end of RT and continue for 2 to 4 weeks, then recover over several weeks.[18,46]

In HNC specific QOL-EORTC HN-35, pain, speech, mouth open and stick saliva were significantly progressed shortly after RT and most symptom scores of QOL did not improve in the follow-up. These acute changes after RT range from oral mucositis, mucosal opportunistic infections, neurosensory disorders to tissue fibrosis.[18 Dry mouth, mouth opening and stick saliva were the most predominant problems in our patients, as Pauli N reported dry mouth and sticky saliva were the major problems in HNC patients, no matter with trismus or not.[4] These long term complication was as Stubblefield MD et al described the radiation fibrosis syndrome (RFS) such as trismus, cervicaldystonia, trigeminal neuralgia, cervical plexus neuralgia, radiculopathy, neuropathy, and myopathy will progressed after radiation.[47] These morbidities all presents in EORTC QLQ-H&N35. It means the QLQ-H&N35 could accurately evaluate the long-term complication of RFS in HNC.

In our study, the limitation is the small number of participants, and the high drop-out rate. The patients fulfilling the protocol to 6 months of follow up is 11 patients, which 9 patients was stage IVa oral cancer and 2 patients were stage I oral cancer. Those patients who completed the duration of follow up had advanced stage disease, who have been more heavily treated and more late effects, giving a sort of selection bias in the results. Further investigations should included large sample size, longer follow-up period and to investigate the early intervention to prevent these morbidities.

CONCLUSION

We should pay more attention to lymphedema because the high prevalence in oral cancer patients even 6-month after RT. Dry mouth, impaired mouth opening, sticky saliva, fatigue and insomnia were the major morbidities. It needs more encouragement in the neck ROM, shoulder abduction and shoulder function in patients who received extensive neck dissection.

REFERENCE

1. Fitzmaurice C, Allen C, Barber RM, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol 2017;3: 524-48.
2. Gogarty DS, Shuman A, O'Sullivan EM, et al. Conceiving a national head and neck cancer screening programme. J Laryngol Otol 2016;130:8-14.
3. Schellenberger ZMTD: The Head and Neck Cancer Patient: Perioperative Care and Assessment, An Issue of Oral and Maxillofacial Surgery Clinics of North America, 1st ed. Philadelphia: Elisvier, 2018;p381-90.
4. Pauli N, Johnson J, Finizia C, et al. The incidence of trismus and long-term impact on health-related quality of life in patients with head and neck cancer. Acta Oncol 2013;52:1137-45.
5. Speksnijder CM, van der Bilt A, Slappendel M, et al. Neck and shoulder function in patients treated for oral malignancies: a 1-year prospective cohort study. Head

Neck 2013;35:1303-13.
6. Short SO, Kaplan JN, Laramore GE, et al. Shoulder pain and function after neck dissection with or without preservation of the spinal accessory nerve. Am J Surg 1984;148:478-82.
7. Sist T, Miner M, Lema M. Characteristics of postradical neck pain syndrome: a report of 25 cases. J Pain Symptom Manage 1999;18:95-102.
8. Benoliel R, Epstein J, Eliav E, et al. Orofacial pain in cancer: part I--mechanisms. J Dent Res 2007;86: 491-505.
9. Epstein JB, Hong C, Logan RM, et al. A systematic review of orofacial pain in patients receiving cancer therapy. Support Care Cancer 2010;18:1023-31.
10. Cramer JD, Johnson JT, Nilsen ML. Pain in Head and Neck Cancer Survivors: Prevalence, Predictors, and Quality-of-Life Impact. Otolaryngol Head Neck Surg 2018;159:853-8.
11. Deng J, Ridner SH, Dietrich MS, et al. Factors associated with external and internal lymphedema in patients with head-and-neck cancer. Int J Radiat Oncol Biol Phys 2012;84:e319-28.
12. Deng J, Ridner SH, Murphy BA. Lymphedema in patients with head and neck cancer. Oncol Nurs Forum 2011;38:E1-E10.
13. Buntzel J, Glatzel M, Mucke R, et al. Influence of amifostine on late radiation-toxicity in head and neck cancer--a follow-up study. Anticancer Res 2007;27: 1953-6.
14. Schiefke F, Akdemir M, Weber A, et al. Function, postoperative morbidity, and quality of life after cervical sentinel node biopsy and after selective neck dissection. Head Neck 2009;31:503-12.
15. Wolff HA, Overbeck T, Roedel RM, et al. Toxicity of daily low dose cisplatin in radiochemotherapy for locally advanced head and neck cancer. J Cancer Res Clin Oncol 2009;135:961-7.
16. Deng J, Ridner SH, Dietrich MS, et al. Prevalence of secondary lymphedema in patients with head and neck cancer. J Pain Symptom Manage 2012;43:244-52.
17. Smith BG, Lewin JS. Lymphedema management in head and neck cancer. Curr Opin Otolaryngol Head Neck Surg 2010;18:153-8.
18. Sroussi HY, Epstein JB, Bensadoun RJ, et al. Common oral complications of head and neck cancer radiation therapy: mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. Cancer Med 2017;6: 2918-31.
19. Wan Leung S, Lee TF, Chien CY, et al. Health-related quality of life in 640 head and neck cancer survivors after radiotherapy using EORTC QLQ-C30 and QLQ-H&N35 questionnaires. BMC Cancer 2011; 11:128.
20. Murer K, Huber GF, Haile SR, et al. Comparison of morbidity between sentinel node biopsy and elective neck dissection for treatment of the n0 neck in patients with oral squamous cell carcinoma. Head Neck 2011;33:1260-4.
21. Teymoortash A, Hoch S, Eivazi B, et al. Postoperative morbidity after different types of selective neck dissection. Laryngoscope 2010;120:924-9.
22. Cancer registry annual report, 2015, Taiwan. https://www.hpa.gov.tw/Pages/Detail.aspx?nodeid=269&pid=10227 Health Promotion Administration, Ministry of Health and Welfare 2017.
23. Földi M, Földi E, Kubik S: Textbook of Lymphology, 2nd ed. München: Urban & Fischer, 2006. p.242.
24. Miller AJ, Bruna J, Beninson J. A universally applicable clinical classification of lymphedema. Angiology 1999;50:189-92.
25. Piso DU, Eckardt A, Liebermann A, et al. Reproducibility of sonographic soft-tissue measurement of the head and neck. Am J Phys Med Rehabil 2002;81:8-12.
26. Piso DU, Eckardt A, Liebermann A, et al. Early rehabilitation of head-neck edema after curative surgery for orofacial tumors. Am J Phys Med Rehabil 2001;80:261-9.
27. Cynthia C. Norkin DJW. Measurement of Joint Motion: A Guide to Goniometry, 2nd ed, Philadelphia: F.A. Davis Company 1995. p.49, 181.
28. Constant CR, Murley AH. A clinical method of functional assessment of the shoulder. Clin Orthop Relat Res 1987:160-4.
29. Chepeha DB, Taylor RJ, Chepeha JC, et al. Functional assessment using Constant's Shoulder Scale after modified radical and selective neck dissection. Head Neck 2002;24:432-6.
30. Fang FM, Chien CY, Kuo SC, et al. Changes in quality

of life of head-and-neck cancer patients following postoperative radiotherapy. Acta Oncol 2004;43: 571-8.

31. Serlin RC, Mendoza TR, Nakamura Y, et al. When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. Pain 1995;61:277-84.
32. Foundation RTOGR. RTOG/EORTC Late Radiation Morbidity Scoring Schema. https://www.rtog.org/ResearchAssociates/AdverseEventReporting/RTOGEORTCLateRadiationMorbidityScoringSchema.aspx; (cited 2019)
33. Deng J, Murphy BA, Dietrich MS, et al. Impact of secondary lymphedema after head and neck cancer treatment on symptoms, functional status, and quality of life. Head Neck 2013;35:1026-35.
34. Erisen L, Basel B, Irdesel J, et al. Shoulder function after accessory nerve-sparing neck dissections. Head Neck 2004;26:967-71.
35. Orhan KS, Demirel T, Baslo B, et al. Spinal accessory nerve function after neck dissections. Journal of Laryngology & Otology 2007;121:44-8.
36. Eickmeyer SM, Walczak CK, Myers KB, et al. Quality of life, shoulder range of motion, and spinal accessory nerve status in 5-year survivors of head and neck cancer. PM R 2014;6:1073-80.
37. Dijkstra PU, Kalk WW, Roodenburg JL. Trismus in head and neck oncology: a systematic review. Oral Oncol 2004;40:879-89.
38. Dijkstra PU, Huisman PM, Roodenburg JL. Criteria for trismus in head and neck oncology. Int J Oral Maxillofac Surg 2006;35:337-42.
39. Ichimura K, Tanaka T. Trismus in patients with malignant tumours in the head and neck. J Laryngol Otol 1993;107:1017-20.
40. Bruns F, Buntzel J, Mucke R, et al. Selenium in the treatment of head and neck lymphedema. Med Princ Pract 2004;13:185-90.
41. Deng J, Ridner SH, Dietrich MS, et al. Assessment of external lymphedema in patients with head and neck cancer: a comparison of four scales. Oncol Nurs Forum 2013;40:501-6.
42. Smith BG, Hutcheson KA, Little LG, et al. Lymphedema outcomes in patients with head and neck cancer. Otolaryngol Head Neck Surg 2015;152: 284-91.
43. Chen MH, Chang PM, Chen PM, et al. Prolonged facial edema is an indicator of poor prognosis in patients with head and neck squamous cell carcinoma. Support Care Cancer 2010;18:1313-9.
44. Ohrn KE, Wahlin YB, Sjoden PO. Oral status during radiotherapy and chemotherapy: a descriptive study of patient experiences and the occurrence of oral complications. Support Care Cancer 2001;9:247-57.
45. Epstein JB, Stewart KH. Radiation therapy and pain in patients with head and neck cancer. Eur J Cancer B Oral Oncol 1993;29B:191-9.
46. Lalla RV, Sonis ST, Peterson DE. Management of oral mucositis in patients who have cancer. Dent Clin North Am 2008;52:61-77.
47. Stubblefield MD, Levine A, Custodio CM, et al. The role of botulinum toxin type A in the radiation fibrosis syndrome: a preliminary report. Arch Phys Med Rehabil 2008;89:417-21.

口腔癌病患放射線治療後之併發症及其對生活品質之影響

唐浩偉[1*] 張東浩[2,3*] 陳冠霖[4] 蔡國陽[5] 廖淑芬[4,6,7] 王偉德[4]

惠來醫療社團法人宏仁醫院復健科[1] 彰化基督教醫院放射腫瘤科[2]
元培科技大學放射系[3] 彰化基督教醫院復健部[4] 彰化基督教醫院口腔外科[5]
彰化基督教兒童醫院兒童復健科[6] 弘光科技大學物理治療系[7]
(*共同第一作者)

研究背景：口腔癌是台灣中年男性最常見的癌症。口腔癌病患最常見的併發症為放射後纖維化症候群和淋巴水腫，此二者會影響病人之生活品質(quality of life)。本研究之目的為以前瞻性研究方式，來追蹤口腔癌病患治療後之常見併發症及其對生活品質之影響。

研究方法：前瞻性追蹤 27 位完成手術及放射線治療之口腔癌病患，在追蹤期間並無接受復健治療。在放射線治療結束時、結束後 3 個月及結束後 6 個月追蹤其疼痛量表(visual analog pain scale, VAS)，淋巴水腫量表，淋巴水腫顏面距離，上下門齒間最大距離(maximal interincisal distance, MID)，肩及頸部活動度(range of motion, ROM)，Constant 肩膀量表(Constant shoulder score)，及歐洲癌症治療與研究組織(EORTC)癌症生活品質核心問卷(QLQ-C30)與頭頸癌生活品質核心問卷(EORTC H-N35)。

結果：肩及頸部活動度還有 Constant shoulder score 在放射線治療結束時是最差。所有受試者均有淋巴水腫，受試者在放射線治療後 6 個月其頸活動度仍有中度受限，肩部外展、內轉、外轉及 Constant shoulder score 肩膀量表仍不足。疼痛量表(4.8±2.1)在放射線治療結束時是最差，同時疼痛指數和淋巴水腫指數($p< 0.001$)、Constant score (Rt- $p= 0.003$,Lt- $p=0.02$)及上下門齒間最大距離($p = 0.049$)有相關。在生活品質方面，疲憊、經濟困難、口乾、張口困難及黏性唾液為最明顯之副作用，在追蹤過程並無明顯改善。

結論：口乾、張口困難、黏性唾液、失眠及淋巴水腫為口腔癌病患手術及放射線治療後最常見長期的併發症。我們需特別注意接受頸部淋巴廓清病患之肩部外展及頸活動度之改善情形。（台灣復健醫誌 2020；48(1)：1 - 13）

關鍵詞：口腔癌(oral cavity cancer)，淋巴水腫(lymphedema)，生活品質(quality of life)，復健(rehabilitation)，放射後纖維化症候群(radiation fibrosis syndrome)

通訊作者：廖淑芬醫師，彰化基督教醫院復健部，彰化縣彰化市 500 南校街 135 號。
電話：(04) 7238595 轉 7439 E-mail：sueliao3@gmail.com doi: 10.6315/TJPMR.202006_48(1).0001