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Correlation between Sternocleidomastoid Muscle Stiffness after Radiation Therapy and Quality of Life in Patients with Head and Neck Cancer

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Original Article

Correlation between Sternocleidomastoid Muscle Stiffness after Radiation Therapy and Quality of Life in Patients with Head and Neck Cancer

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Objective: Radiation-induced fibrosis after radiation treatment frequently results in neck and shoulder pain/dysfunction, trismus, dysphagia, muscle stiffness and lower health-related quality of life (HRQOL) in patients with head and neck (H&N) cancer. Here, we access the correlation between neck muscle stiffness after radiation therapy and HRQOL, and the effect of rehabilitation on muscle stiffness and HRQOL.

Method: We used real-time sonoelastography to evaluate sternocleidomastoid muscle (SCM) stiffness after radiation therapy. We used the EORTC QLQ-30 and EORTCQLQ H&N35 to evaluate the HRQOL of H&N cancer patients. Each participant received real-time sonoelastography and an HRQOL evaluation twice with the course of 6 months to compare changes in soft-tissue stiffness and HRQOL. The participants were subdivided into two groups with and without rehabilitation treatment to compare the effect of rehabilitation on changes in SCM stiffness and HRQOL.

Results: Twenty-five patients with H&N cancers were included in the study. Seventeen of the patients completed both evaluations 6 months later. The SCM stiffness area of the radiation site was significantly larger than the non-radiation site at the initial evaluation (54.3 ± 23.0 % vs. 40.5 ± 19.7 %, p=0.036), but the SCM stiffness area of both sites showed no significant difference 6 months after the initial evaluation. Some of the HRQOL subscales (physical functioning, emotion functioning, nausea/vomiting, dyspnea, insomnia and senses problems) improved when the SCM stiffness area decreased at follow up. The SCM stiffness area and HRQOL changes were not significantly different for patients with or without the rehabilitation treatment, which may be due to the small number of participants in our study.

Conclusions: The HRQOL of H&N cancer patients revealed a negative correlation with the SCM stiffness area change. Rehabilitation treatment showed no significant effect on the SCM stiffness area change and HRQOL, which may be due to the small number of participants and variations in compliance with rehabilitation treatment in our cohort. (Tw J Phys Med Rehabil 2015; 43(4): 203 - 216)

Key Words: head and neck cancer, sternocleidomastoid muscle stiffness, sonoelastography, health-related quality of life

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INTRODUCTION

In Taiwan, the head and neck (H&N) cancer is the sixth most common cancer, and the incidence of newly diagnosed H&N cancer cases increased to approximately 5.03% annually.[1] The five-year survival rate of patients with H&N cancer also increased from 38.9% to 55.8% in the past 20 years.[2] Because of the improved survival rate of patients with H&N cancer, the impact of the disease and treatment modalities on health-related quality of life (HRQOL) in long-term survivors with H&N cancer is increasingly a concern for healthcare providers.[3-5] Factors associated with lower HRQOL that have been reported include age, depression, decreased body mass index, gastrostomy, disease specific functional impairment and a history of radiation therapy.[3,4,6,7] Approximately 36-83% of all patients with H&N cancer in Taiwan received radiation therapy (including radiation only, surgery with radiation therapy and chemo-radiation therapy).[1] Studies have reported the impact of different treatment modalities on HRQOL of patients with H&N cancer,[4,8,9] but there is a paucity of studies about how radiation therapy impacts HRQOL. Soft tissue injuries induced by radiation include fibrosis and necrosis,[10,11] which may cause neck and shoulder pain, muscle weakness and stiffness, dry mouth, trismus and dysphagia in patient with H&N cancer.[10,12] In this article, we report the correlation between the severity of sternocleidomastoid (SCM) stiffness after radiation therapy and the HRQOL of patients with H&N cancer; we also report the effect of rehabilitation treatment on changes in muscle stiffness and HRQOL in H&N cancer patients.

METHODS

Participants

Patients with a first diagnosis of H&N cancer aged 20-80 years old who received radiation therapy in the medical center were included in this study. Exclusion criteria included: (1) patients with recurrent tumors or individuals with more than one kind of tumor, (2) patients with consciousness disturbances or individuals who could not express their own will, (3) patients who could not complete the muscle stiffness evaluation or the HRQOL evaluation, (4) patients with acute systemic inflammation or infection (e.g., pneumonia, sepsis), or (5) patients with another major disease (e.g., stroke, motor neuron degeneration disorders, traumatic brain injury, etc.). Informed consent was obtained from the patients prior to the initiation of the study.

Evaluation of SCM stiffness

We evaluated the severity of SCM stiffness using real-time sonoelastography (Acuson Antares 5.0, Simens, USA, 8.89MHz, linear probe). The real-time sonoelastography is a color-coded elastogram superimposed over the B-mode sonogram (Figures 1A & B). The soft tissue stiffness is represented by different colors in the region of interest (ROI) ranging from red (very hard), yellow (hard), green (medium hardness) and blue to purple (soft). We calculated the percentage of red and yellow (very hard and hard) areas in the ROI (upper third of sternocleidomastoid muscle, SCM) using Adobe Photoshop CC (Adobe Systems Incorporated, Ireland) of both sides of the neck, and these data were selected to represent the degree of soft tissue stiffness. The side of the neck that received the radiation treatment is referred to as the “radiation site”, and the side of the neck that did not receive the radiation treatment is referred as the “non-radiation site”. If the patient received radiation therapy on both sides of his or her neck, both sides were referred to as the “radiation site”.The sonoelastography was performed by the same physician with 8 years’ experience of musculoskeletal ultrasound examination. No compression applied to the soft tissue during the real-time sonoelastography examination.

Health-related quality of life

The HRQOL of the H&N cancer patients were evaluated by The European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck Cancer Module (EORTCQLQ H&N35).[13,14] The QLQ-C30 includes five functional scales, three symptom scales and a global health status; the H&N35 module includes 18 symptom scales. The questionnaires were answered by the partici-

pants themselves. We then transformed the raw data to scores ranging from 0 to 100. A high score on a functional scale or health status represented a high level of function or quality of life, but a high score on a symptom scale represented a severe problem.

Rehabilitation program

Rehabilitation programs (including physical therapy and speech-language therapy) were arranged for all of the subjects in our cohort. However, because of some confounding factors (e.g. location and transportation problems, time issues), some subjects were unable to participate in the rehabilitation programs. We accordingly subdivided the subjects into two groups on the basis of participation in the rehabilitation program to compare the effect of rehabilitation on muscle stiffness after radiation therapy and HRQOL.

The initial results of the sonoelastography examination and the HRQOL evaluation after the completion of radiation therapy are referred as the baseline data. These data were followed up again 6 months later (the follow-up data).

Data analysis and statics

We performed statistical analyses using SPSS 21 (IBM corp. USA). We used the Wilcoxon-Mann-Whitney U test to assess the differences in radiation dose and muscle stiffness area between the surgical and the non-surgical areas; we used the Wilcoxon signed-rank test to assess the differences in the muscle stiffness area change between the radiation and non-radiation sites and the area change between the baseline and follow-up examinations. We set the significance level at $p<0.05$. A change in HRQOL score of more than 10 points was recognized as a significant clinical change.[5,15,16]

RESULTS

Twenty-eight participants were referred from radiation-oncology department for real-time sonoelastography examination and HRQOL evaluations. Three of the participants were excluded from the study because of recurrent H&N tumors. The remaining 25 participants (23 males, 2 females) all completed the baseline sonoelastography examination and HRQOL evaluation. At follow up, 17 participants complete the sonoelastography examination and the HRQOL evaluation. The reasons for patient attrition from the study included the death of one participant and concerns pertaining to transportation of the others. The sonoelastography results at baseline and follow up are shown in Tables 1 and 2, and the HRQOL results at baseline and follow up are shown in Figures 2 and 3.

The percentage of the SCM stiffness area of the radiation site at the baseline and follow up did not vary significantly between patients with and without surgical intervention (Table 1; without surgery 43.6 ± 19.3% vs. with surgery 60.4 ± 23.2%, p=0.057 at baseline; without surgery 26.7 ± 15.1% vs. with surgery 45.7 ± 28.6%, p=0.296 at follow up). However, patients who did not undergo surgery received a higher radiation dose than patients that underwent surgery (72.5 ± 1.8 Gy vs. 70.3 ± 11.7 Gy, p=0.004).

At baseline, the percentage of muscle stiffness area in the radiation site was higher than the percentage of stiffness area in non-radiation sites (Table 2, 54.3 ± 23.0 % vs. 40.5 ± 19.7 %, p=0.036), but at follow up there was no significant statistical difference in the percentage of muscle stiffness area between radiation and non-radiation sites (Table 2, 41.2 ± 26.9 % vs. 33.1 ± 23.1 %, p=0.155).

In terms of the QLQ-C30 questionnaire, only the global health status was associated with clinically significant improvement at follow up (41.7 ± 18.9 vs. 60.8 ± 20.6 at baseline and follow up; mean difference19.2 ± 26.8, p=0.008, Figure 2A). The other functional scales and symptom scales of the QLQ-C30 showed no significant clinical change at follow up (Figures 2A & B). The EORTCQLQ H&N35 revealed that dry mouth was worse at follow up (56.9 ± 32.9 vs. 70.6 ± 26.1 at baseline and follow up; mean difference 13.7 ± 35.5, p=0.019, Figure 3B). There were also fewer instances of feeding tube (58.8 ± 50.7 vs. 29.4 ± 47.0 at baseline and follow up, mean difference -29.4 ± 47.0, p=0.025) and more weight gain (23.5 ± 43.7 vs. 35.3 ± 49.3 at baseline and follow up; mean difference 18.8 ± 40.3, p=0.037) at follow up (Figure 3B). The other problem scales in the H&N35 showed no significant clinical difference at follow up (Figures 3A & B).

In order to compare the impact of muscle stiffness change and rehabilitation treatment on the HRQOL at

follow up, we further subdivided the HRQOL status into clinically "Worse" (a score decreased of at least 10), "No change" (a score change between -9 and 9) and "Better" (a score improvement of more than 10). In Figure 4A & B, one can see that the SCM stiffness area change at follow up exhibited a significant negative correlation with physical functioning (r=-0.493, p=0.022), emotional functioning(r=-0.464, p=0.030), nausea/vomiting (r=-0.491, p=0.023), dyspnea (r=-0.611, p=0.005), insomnia (r=-0.471, p=0.028) and senses problems (r=-0.577, p=0.008) status changes, which means that a decrease in SCM stiffness accompanied with an improvement in HRQOL status. For the 17 participants who completed follow up, the change in HRQOL status (Figure 5A & B) between patients with and without rehabilitation treatment (i.e., patients who received more than 3 sessions of rehabilitation treatment vs. patients who did not receive a rehabilitation program or only received fewer than 3 sessions of rehabilitation treatment) was not statistically significant. The muscle stiffness area changes of radiation site between patients with and without rehabilitation treatment also showed no significantly statistical difference (Table 2).

Table 1. Patients data and sonoelastography

	Without Surgery	With Surgery	p value
Baseline (n=25)			
Gender			
Male	8	15	
Female	1	1	
Age (years)	53.4 ± 11.4 (40.9~78.8)	53.9 ± 7.8 (42.6~71.2)	0.637
Radiation dose (Gy)	72.5 ± 1.8 (median: 72.0; range70.0~74.8)	70.3 ± 11.7 (median: 68.0; range64.0~112.8)	0.004
Stiffness area* (%)	43.6 ± 19.3 (18.8~80.3)	60.4 ± 23.2 (8.0~88.6)	0.057
Duration after radiation therapy (day)	117.7 ± 94.0 (0~264)	82.5 ± 70.5 (15~232)	
Follow up (n=17)			
Gender			
Male	4	12	
Female	0	1	
Stiffness area* (%)	26.7 ± 15.1 (6.9~42.2)	45.7 ± 28.6 (5.6~85.8)	0.296
Duration at follow up (day)	197 ± 46.9 (161~281)	198.7 ± 12.0 (187~211)	

*Stiffness area of radiation site

Table 2. Stiffness area change of radiation and non-radiation site

	Radiation site	Non-radiation site	p value
Baseline	(25 sites)	(15 sites)	
Stiffness area (%)	54.3 ± 23.0	40.5 ± 19.7	0.036
Follow up	(17 sites)	(11 sites)	
Stiffness area (%)	41.2 ± 26.9	33.1 ± 23.1	0.155
Stiffness area change (%)			
-R	-23.5 ± 33.1		1.0
+R	-18.3 ± 31.6		

-R: non-rehabilitation group. Participants did not receive a rehabilitation treatment or received less than 3 sessions of rehabilitation treatment.

+R: rehabilitation group.Participants received more than 3 sessions of rehabilitation treatment.

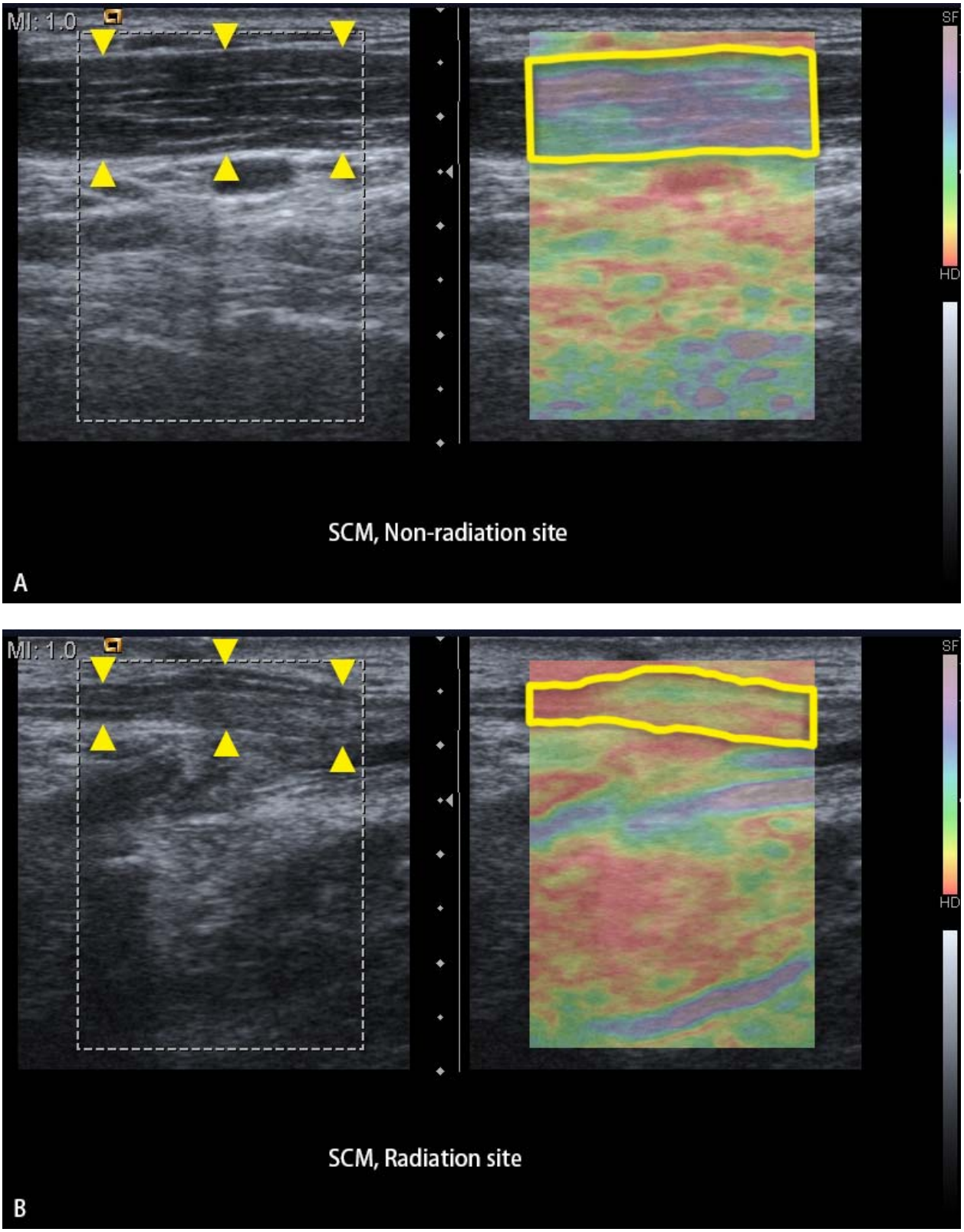


Figure 1. Real-time sonoelastography. (A) non-radiation site, (B) radiation site. The yellow arrow heads of B-mode sonogram (left side panel) mark the area of SCM, the yellow frame of color-coded sonogram (right side panel) mark the range for calculating the red and yellow area.

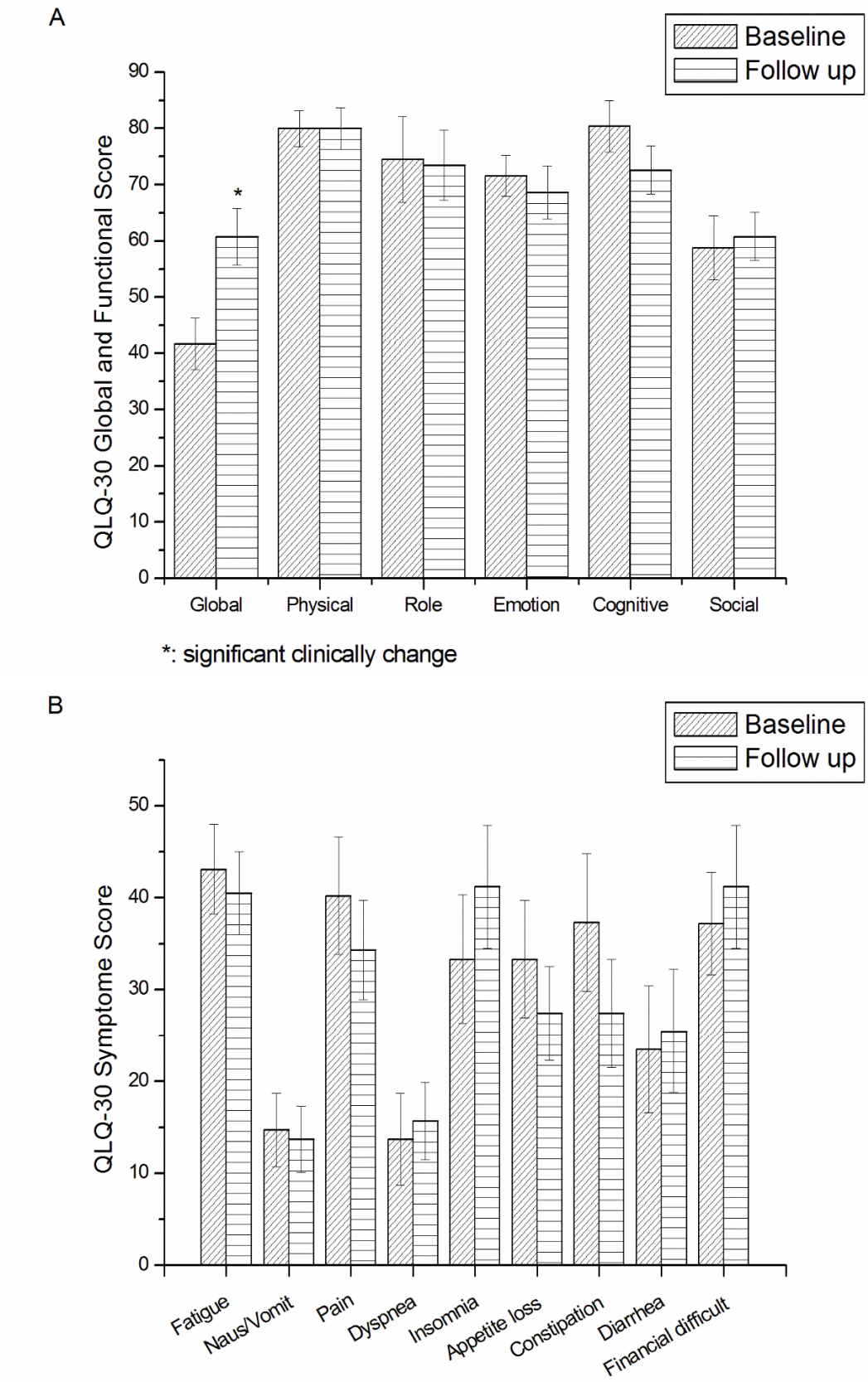


Figure 2. Baseline and follow up values of QLQ-C30. (A) global-health and functional scale, (B) symptom scales. Score changes more than 10 points is referred as significant clinically change. "*" marks as significant clinically change.

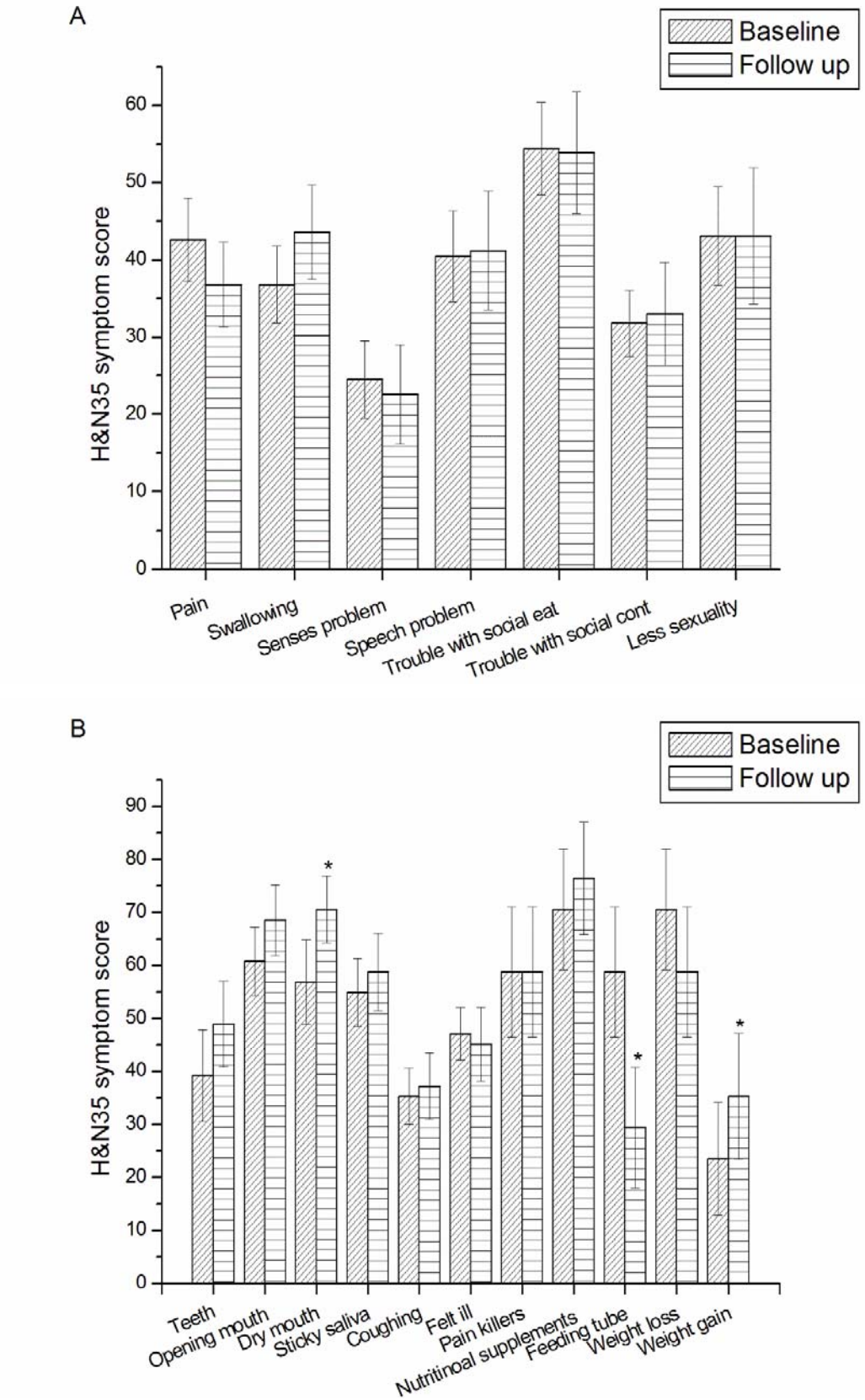
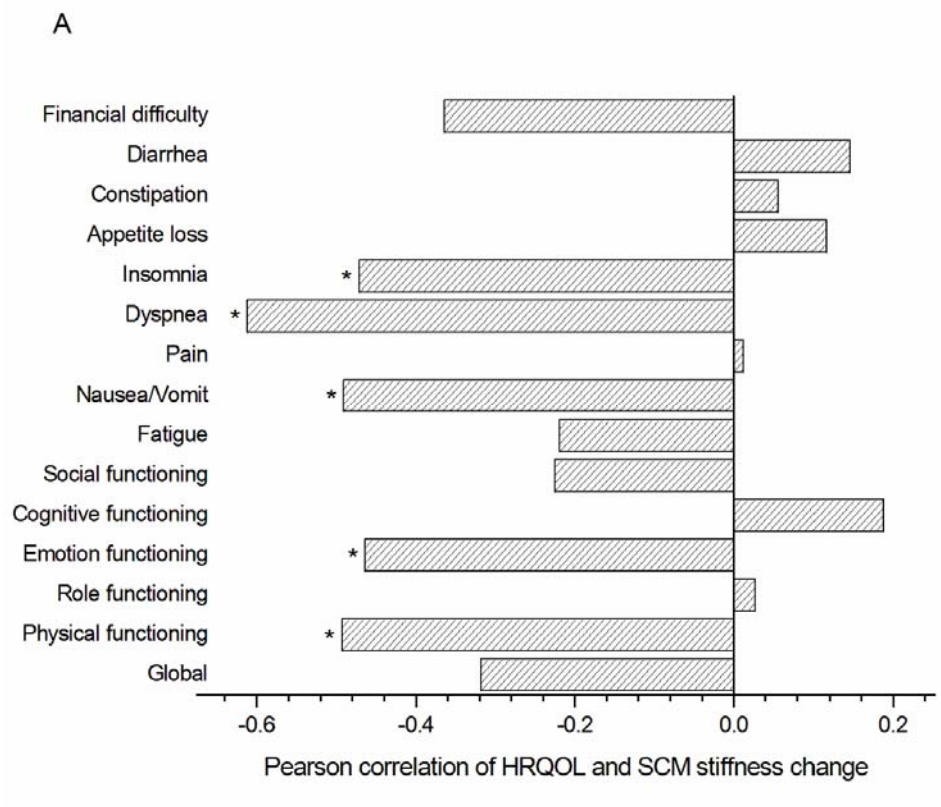


Figure 3 A and B. Baseline and follow up values of EORTCQLQ H&N35 symptom score. Score changes more than 10 points is referred as significant clinically change. "*" marks as significant clinically change.



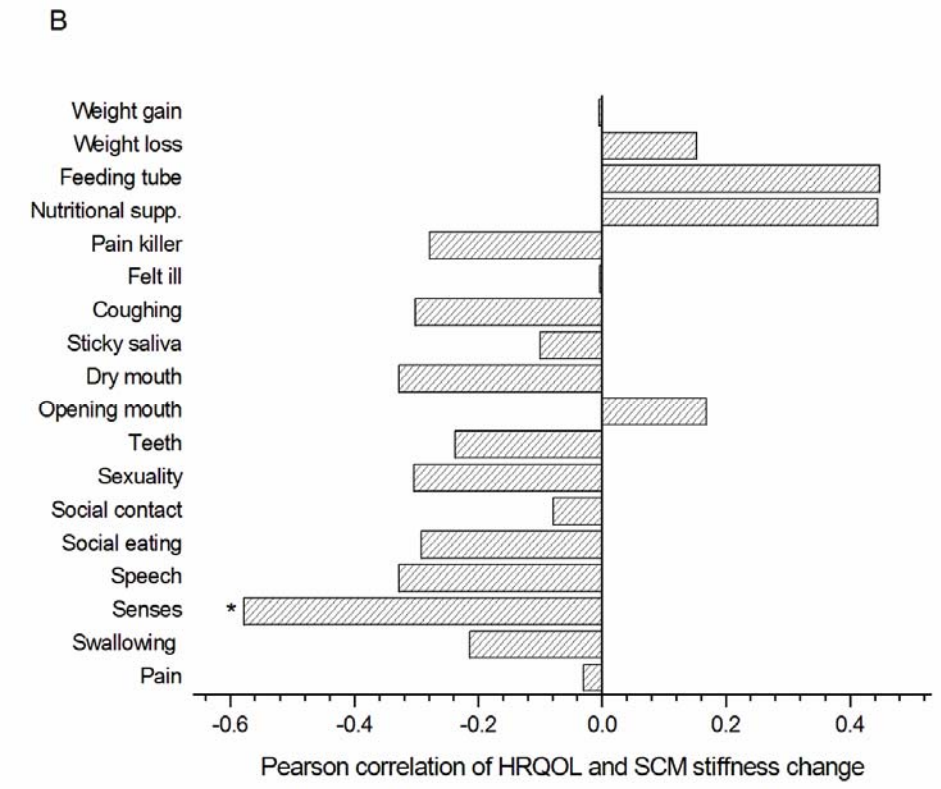
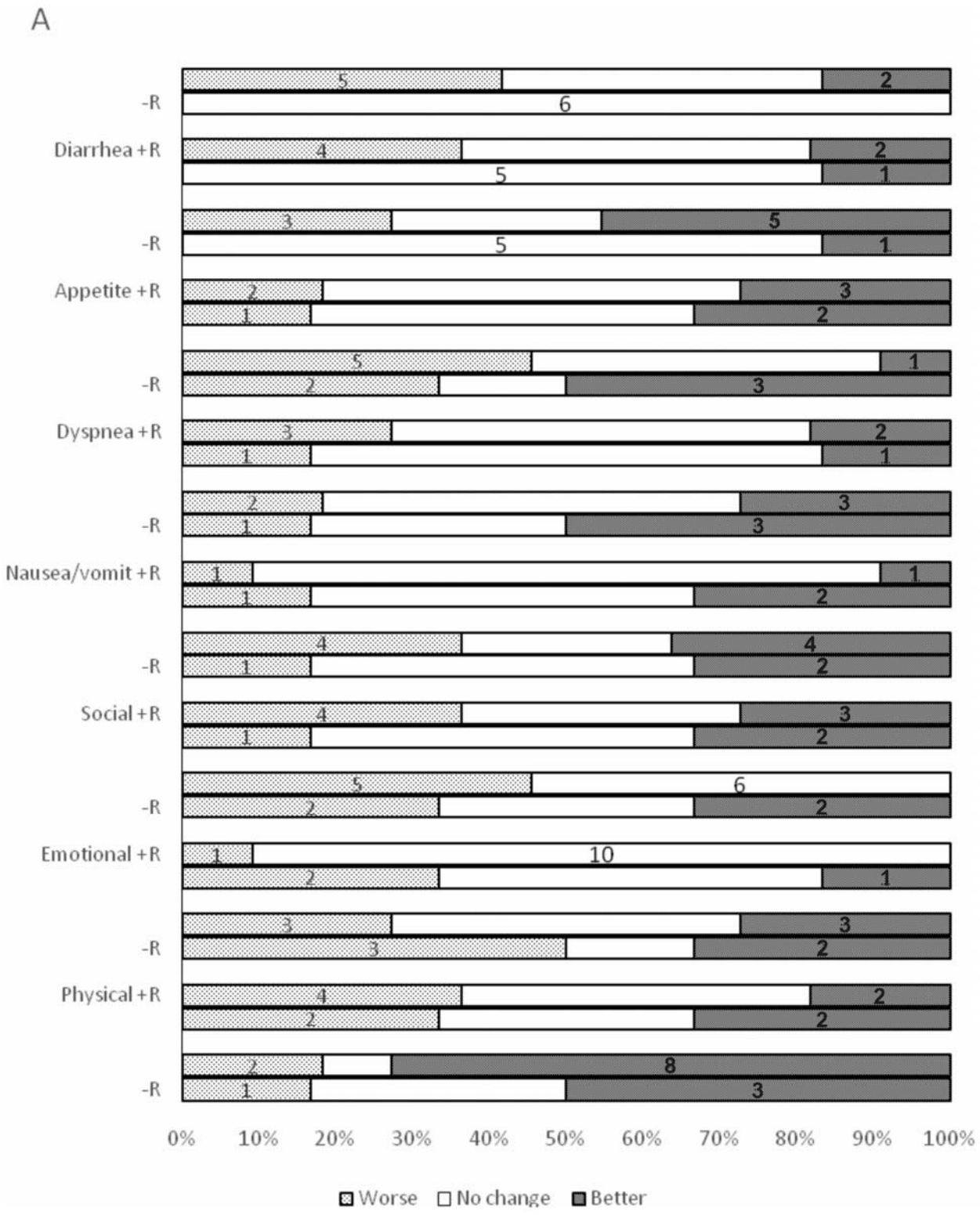


Figure 4 A and B. Correlations between SCM stiffness change and HRQOL change. (A) QLQ-30 subscales, (B) H&N35 subscales. "*" marks as $p<0.05$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Diarrhea +R
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Appetite +R
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Dyspnea +R
-R
Nausea/vomit +R
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Social +R
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Emotional +R
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Physical +R
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Worse
No change
Better

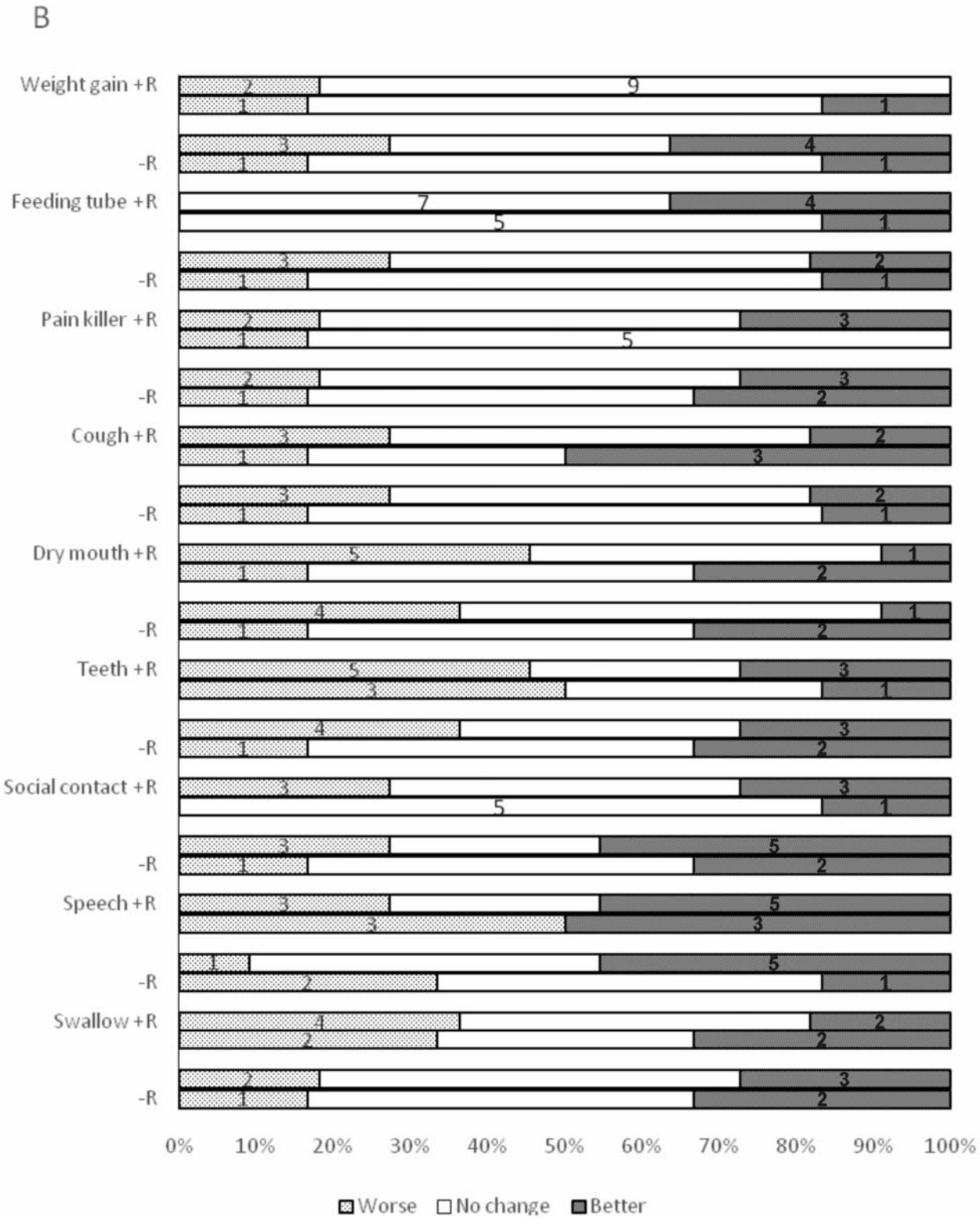

Figure 5 A and B.Correlations of HRQOL change between participants with and without rehabilitation treatment. (A) QLQ-30 subscales, (B) H&N35 subscales. Results showed no significantly HRQOL difference between participants with and without rehabilitation treatment. Numbers in the bars represent case numbers. (+R: rehabilitation group, n=11; -R: non-rehabilitation group, n=6)

DISCUSSION

Real-time sonoelastography had been used to evaluate soft tissue elasticity such as liver cirrhosis, differentiate between malignant and benign breast cancer, glandular disease and musculoskeletal diseases.[17-19] It provides clinicians with real-time information about normal and abnormal elasticity of soft tissues. Kwon and Park have reported the application of real-time sonoelastography to evaluate the SCM stiffness in infants with congenital muscular torticollis.[20,21] To the best of our knowledge, this investigation is the first study to evaluate SCM stiffness after radiation therapy using real-time sonoelastography.

Although our study revealed that patients who did not receive surgical intervention received a higher radiation dose at the site of treatment than individuals who received surgical intervention (Table 1), the change in SCM stiffness areas showed no significant difference between the surgical and non-surgical group at the baseline and at follow up (Tables 1 and 2). These results mean that the degree of SCM stiffness in the ROI were not influenced by the surgical process in this study; and the other possible reason for the results is that the difference of radiation dose between both groups (surgical and non-surgical) has no significant effect on the muscle stiffness change.

At baseline, the mean SCM stiffness area was larger at the radiation sites than that at the non-radiation sites (Table 2;54.3 ± 23.0% vs. 40.5 ± 19.7%, $p<0.05$), but at the follow-up stage the mean SCM stiffness area showed no statistically significant difference between these two sites. These results hint that the degree of SCM stiffness improved 6 months after the initial evaluation. Delanian and Lefaix[11] have reported 3 phases of histopathological change in radiation-induced fibrosis: (1) a pre-fibrotic phase (chronic inflammation and often asymptomatic), (2) organized fibrosis (patchwork of areas of active fibrosis), and (3) a late fibroatrophic phase (retractile fibrosis and gradual loss of parenchymal cells). These histopathological changes occur over several years, but the authors did not note how long each process took. Because our follow-up duration was only 6 to 9 months, longer periods of follow up for SCM stiffness changes should be considered in future studies.

Previous reports have shown that the HRQOL of H&N cancer patients was significantly lower than normal populations at diagnosis and 6 months after follow up. However, these same studies showed that these function and problem scores returned to their pretreatment value within the first year.[3,5,22] The lower scores were largely with to treatment-related side effects (such as dysphagia, dry mouth, trismus) and disease specific problems (such as fatigue, anxiety and pain). Our results were similar although we did not make comparisons with a normal population (we compared with the patient themselves). At follow up the global-health status (including the health status and quality of life rated subjectively by the patients themselves) of our participants exhibited a significantly clinical improvement at 6 months. At the same time, the patients also used feeding tubes less frequently, and they gained more weight. However, their dry mouth symptoms worsened (Figures 2 and 3). These findings suggest that the general conditions of the participants improved after 6 months of follow up, but some of treatment-specific problems (i.e., dry mouth after radiation therapy) were worse at follow up.

Studies have revealed that exercise and rehabilitation have positive effects on improving the overall HRQOL, oral function, swallowing function, anxiety and pain of cancer patients.[23-26] In this study, we hypothesized that a rehabilitation program would improve the HRQOL of H&N cancer patients after radiation therapy, but our results showed no significant HRQOL change between patients who received or did not received rehabilitation treatment (Figure 5A & B). This finding may be due to the small number of participants who received rehabilitation treatment (n=11), and the other possible reason is large variations in the numbers of rehabilitation treatment sessions among each participant (6 to 82 sessions) in the rehabilitation group due to different compliance with the rehabilitation treatment. We need to examine a larger cohort of participants in the future.

Although the rehabilitation program showed no statistically significant effect on HRQOL, SCM stiffness changes were correlated with some of the change in the HRQOL subscales. The physical functioning, emotional

functioning, nausea/vomiting, dyspnea and insomnia subscales of the QLQ-30 improved when SCM stiffness decreased at follow up; the senses problem subscale of the EORTCQLQ H&N35 improved when SCM stiffness decreased at follow up (Figure 4A & B). Radiation-induced fibrosis may cause neck/upper back pain and weakness and shoulder pain/dysfunction due to nerve injury and myopathic changes. These problems can then cause discomfort, affect swallowing ability, and result in problems performing daily activities and work.[10,27] Therefore, it is reasonable that physical functioning and psychological conditions will improve if soft tissue stiffness improve, as was shown by our results. Although the general HRQOL of H&N cancer patients improved when SCM stiffness decreased, most of the H&N cancer-specific HRQOL (EORTCQLQ H&N35) subscales showed no significant correlation with SCM stiffness change except for the senses problems subscale (Figure 4B). The H&N cancer-specific subscales are mostly related to swallowing problems, speech problems, oral/pharyngeal pain, dry mouth/sticky saliva, etc.These symptoms are largely due to vital structures of head and neck involvement (such as the brachial plexus, masseter muscles, trapezius muscles, SCM, rotator cuffs, salivary glands, etc.)[10] caused by radiation treatment. In this study, the soft tissue stiffness examination did not include most of the vital structures noted above but only the SCM. This fact may be the reason why the SCM stiffness change detected in this study was not significantly correlated with the H&N cancer-specific HRQOL change.

CONCLUSION

SCM stiffness of H&N cancer patients in creased significantly after radiation treatment, but it improved 6 months later. HRQOL subscales such as physical functioning, emotional functioning, nausea/vomiting, dyspnea, insomnia and senses problems improve as SCM stiffness decreases. The HRQOL and SCM stiffness changes showed no significant correlation with the rehabilitation program, which may be due to the small number and different compliance with rehabilitation treatment of participants in our study.

STUDY LIMITATIONS

The soft tissue stiffness evaluation in this study did not include the entire area of the radiation treatment but only upper third of the SCM. This fact could be the primary reason why the soft tissue stiffness changes was not correlated with the H&N cancer-specific HRQOL subscales change. A larger extent of vital structures stiffness of the H&N should be included in future studies. The percentage of stiffness area was calculated by the red and yellow color distribution of sonoelastography in the ROI, which was a semi-quantitative method for the evaluation of SCM stiffness but not an absolute value of muscle stiffness. Shear-wave sonoelastography for quantitative muscle stiffness evaluation is considered in the future study. Furthermore, our small number of participants and large variations of rehabilitation treatment sessions are other limitations of this study. We need additional participants and better compliance in rehabilitation treatment to evaluate positive changes in the HRQOL of H&N patients after radiation treatment.

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頭頸癌患者放射治療後胸鎖乳突肌硬化與生活品質之關係

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研究目的：頭頸癌患者接受放射治療後之軟組織纖維化經常造成疼痛、口乾、進食障礙及肩頸功能障礙及肌肉硬化等。本研究希望了解肌肉硬化程度與生活品質之關係，及復健治療是否可改善肌肉硬化程度及生活品質。

研究方法：頭頸癌患者接受放射治療後，以彈力超音波(real-time sonoelastography)檢測胸鎖乳突肌硬化程度，以 EORTC QLQ-35 及 EORTCQLQ H&N35 來評估患者之健康相關生活品質(health-related quality of life)。6 個月後再次比較胸鎖乳突肌硬化程度及生活品質之改變，並同時比較患者有、無接受復健治療對胸鎖乳突肌硬化程度及生活品質的影響。

結果：本研究共有 25 位頭頸癌患者參與，最後共有 17 位患者完成追蹤。放射治療區域胸鎖乳突肌硬化程度明顯高於對照區域(54.3 ± 23.0 % vs. 40.5 ±19.7 %, p=0.036)，但 6 個月後兩者則無顯著差異。當胸鎖乳突肌硬化程度改善時，身體功能、情緒功能、噁心/嘔吐、呼吸困難、失眠及感覺障礙等生活品質也隨之改善。而患者有無接受復健治療則與胸鎖乳突肌硬化程度及生活品質之改變無顯著相關，可能是因受試人數太少及個案接受復健治療次數差異較大所致。

結論：頭頸癌患者放射治療部位之胸鎖乳突肌硬化程度改善後，生活品質也會隨之改善；而胸鎖乳突肌硬化程度及生活品質之改變程度則與復健治療無顯著相關，可能是因受試人數不足及復健治療次數差異所致，日後仍需收集更多患者以再次分析復健之成效。（台灣復健醫誌 2015；43(4)：203 - 216）

關鍵詞：頭頸癌(head and neck cancer)，胸鎖乳突肌硬化(sternocleidomastoid muscle stiffness)，彈力超音波(sonoelastography)，健康相關生活品質(health-related quality of life)

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