ACTA ONCOLOGICA
2022, VOL. 61, NO. 2, 134–140
https://doi.org/10.1080/0284186X.2021.2022198

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Swallowing sparing intensity modulated radiotherapy versus standard parotid sparing intensity-modulated radiotherapy for treatment of head and neck cancer: a randomized clinical trial

May Gamal Ashour[a], Tarek Hamed Shouman[a], Ashraf Hamed Hassouna[a], Maha Hassan Mokhtar[b], Reem Emad El Din[a], Ayda Aly Youssef[c], Mohammed Mohammed Gomaa[c] and Shaimaa Abdelgeleel[d]

[a]Radiation Oncology Department, National Cancer Institute Cairo University, Cairo, Egypt; [b]Physics Unit, National Cancer Institute Cairo University, Cairo, Egypt; [c]Radiology Department, National Cancer Institute Cairo University, Cairo, Egypt; [d]Statistics Department, National Cancer Institute Cairo University, Cairo, Egypt

ABSTRACT

Background: Dysphagia is a distressing symptom during and after radiotherapy treatment in head and neck cancer (HNC) patients. The objective of this prospective study was to investigate whether swallowing sparing intensity modulated radiotherapy (SW-IMRT) reduces the occurrence of swallowing dysfunction compared to the standard IMRT (ST-IMRT).

Methods: We randomized, planned, and treated patients with HNC who needed whole neck irradiation using the simultaneous integrated boost (SIB) IMRT technique. Doses of 70, 60, and 54 Gy (over 33 daily fractions) were prescribed to the primary tumor, high-risk and low-risk regions, respectively. The postoperative cases received 60 and 54 Gy (over 30 daily fractions) to the high-risk planning target volume (PTV) and low-risk PTV. We contoured organs at risk related to swallowing dysfunction (SWOARs) in all cases. In the ST-IMRT group, parotids only were spared. In the SW-IMRT group, parotids and SWOARs outside the high-risk PTV were spared. Assessment of dysphagia included clinical and instrumental evaluation.

Results: One hundred forty-six patients ended their radiotherapy treatment. Dose distribution showed comparable PTV coverage and no difference in parotid glands sparing between the two groups. SWOARs dose reduction with SW-IMRT differs according to tumor location and its overlap with SWOARs. Using different assessment methods, SW-IMRT was associated with a lower occurrence of dysphagia up to one year after treatment. There was no difference between the two groups regarding acute dysphagia ($p = 0.262$), overall survival ($p = 0.811$), and disease-free survival ($p = 0.876$).

Conclusion: SW-IMRT is significantly better than ST-IMRT regarding a physician-rated and objective assessment of swallowing dysfunction at short- and long-term post-treatment follow-up.

ARTICLE HISTORY
Received 2 May 2021
Accepted 21 October 2021

KEYWORDS
Head and neck cancer; ST-IMRT; SW-IMRT; dysphagia; SWOARs

Background

For the past decade, advances have been made in HNC treatment. Increased treatment intensity, either through concurrent radiotherapy and chemotherapy or altered fractionation schedules, improves tumor control and survival [1]. However, this comes at the cost of increased acute and late effects, significantly impacting function and quality of life (QOL). HNC appears in structurally complex areas that function may be impaired due to disease or treatment [2].

Due to the inverse planning IMRT technique, organs not listed as avoidance structures can receive higher doses than expected [3]. Dysphagia is one of the leading complications that impair QOL during and after radiotherapy. Clinical trials have been conducted to determine the association between irradiated structures and dysphagia [4]. SW-IMRT is a new concept following parotid sparing IMRT to reduce the dose to muscles related to dysphagia [5]. The absence of phase-III clinical trials demonstrating SW-IMRT superiority prevents its integration into routine clinical practice.

Therefore, this study aimed to clinically demonstrate whether SW-IMRT can decrease the occurrence of swallowing dysfunction compared to the standard parotid sparing ST-IMRT.

Patients and methods

This prospective randomized trial included 146 patients with head and neck squamous cell carcinoma from September 2015 to December 2018. The study was approved by the Ethical Review Board of the National Cancer Institute (Approval no.: MD201001409.3).

The study was registered on Clinical Trials.gov (NCT04597177). All patients signed informed consent before initiation of the treatment and we used the CONSORT reporting guidelines.

CONTACT May Gamal Ashour may.ashour@nci.cu.edu.eg Radiation Oncology Department, National Cancer Institute Cairo University, Cairo, Egypt
Supplemental data for this article can be accessed here.

Inclusion criteria were age 18 years or more, oral cavity, pharynx, or laryngeal squamous cell carcinoma requiring whole neck irradiation as a part of definitive or adjuvant radiotherapy (RT) alone or combined with chemotherapy, WHO performance status 0 or 1, and available for long-term follow-up. Patients who had previously received head and neck radiotherapy, prior neoplasms, and/or distant metastases were excluded from the study.

Patients were grouped according to the 2010 staging nomenclature of the American Joint Committee on Cancer Staging Manual (AJCC) Seventh Edition. All patients were subjected to PET-CT before simulation for fusion with contrasted CT scan with 2.5 mm slice thickness. Target volume definition was done according to the tumor site. The gross tumor volume (GTV) delineation was created using clinical information, CT/MRI, and Positron Emission Tomography–Computed Tomography (PET/CT) threshold of 40%. Delineation of SWOARs was performed according to CT-based delineation protocols, including pharyngeal constrictor muscles (PCM); superior (SPC), middle (MPC), inferior (IPC), cricopharyngeus muscle, esophageal inlet muscle (EIM), cervical esophagus, the base of the tongue, and glottic and supraglottic larynx (SGL) [6].

All patients were treated by SIB- IMRT technique. Doses of 70, 60, and 54 Gy (over 33 daily fractions) were prescribed to the primary tumor, high-risk and low-risk regions, respectively, in radical cases. In the postoperative cases, 60 and 54 Gy (over 30 daily fractions) were given to high-risk planning target volume (PTV) and low-risk PTV. All patients were optimized for parotid sparing IMRT using the Monaco software planning system's step and shoot technique (Elekta, Stockholm, Sweden). Then, the patients were randomly assigned to either the standard parotid sparing IMRT (ST-IMRT group, $n = 75$) or swallowing sparing IMRT (SW-IMRT group, $n = 71$) using a computer-generated randomization schedule and sealed opaque envelope technique. The SW-IMRT group received a second optimization to spare the SWOARs outside the high-risk PTV by introducing them as OARs in the treatment planning objectives. Dose reduction with SW-IMRT differs according to tumor location and its overlap with SWOARs. SWOARs dose constraints used are available in Supplementary data Table 1. Image-guided radiotherapy (IGRT) using cone-beam CT images was done weekly for all patients.

Assessment of treatment results

Toxicity and response assessment: NCI Common Terminology Criteria for Adverse Events (CTCAE) v4 [7] was used to assess acute dysphagia. The patients were evaluated weekly during RT and one month after completing treatment regarding dysphagia and xerostomia. Imaging response was evaluated using PET-CT three months after RT. Then, imaging was done regularly every six months. Late toxicity was reported using RTOG/EORTC late radiation morbidity [8]. Survival data were assessed at three months and up to three years post-treatment. Objective swallowing outcome was evaluated in a subset of patients using Video fluoroscopy at three, six months, and one year after treatment using dynamic imaging grade of swallowing toxicity (DIGEST) scale [9]. The patients who developed local recurrence or distant metastases were then excluded from follow up.

Sample size estimation

According to a study done by Feng *et al.* [10], mean doses to the whole PCM and, in particular, the SPC had the highest correlations with aspiration. None of the nine patients received mean PCM doses of 60 Gy aspirated (SW-IMRT), while 16 of the 26 patients received mean PCM doses >60 Gy aspirated (ST-IMRT). We can see that difference if we recruit at least 26 patients per arm, knowing that test will be two-tailed with a power not exceeding 80% and 95% confidence level.

Statistical methods

REDCap research electronic data collection software V6.10.12 (Radiation Oncology Record, Vanderbilt University, Nashville, Tennessee, USA) collected and managed study data. Statistical analysis was done using IBM SPSS® Statistics version 23.

As appropriate, numerical data were expressed as mean and standard deviation or median and range. Frequency and percentages were used to express qualitative results. The relationship between qualitative variables was examined using Pearson's Chi-square or Fisher's exact test. For quantitative results, the t-test was used to compare two groups. The Kaplan-Meier approach was used to do the survival analysis. Overall survival was calculated from the date of diagnosis until the date of death or the last follow-up. Disease-free survival was calculated from the end of treatment till the date of recurrence, death, or last follow-up. Recurrence-free survival was calculated from the end of radiotherapy till the date of recurrence. The log-rank test was used to compare survival curves. All tests were two-tailed. A p-value < 0.05 was considered significant.

Results

One hundred and forty-six patients completed RT (Figure 1). The primary tumor site is shown in Table 1. Stage III was the most common ($n = 66$, 45.2%), followed by stage IV ($n = 61$, 41.8%). Other patient and treatment characteristics are shown in Table 1.

Dose distribution showed comparable PTV coverage and no difference in parotid glands sparing between the two groups. Also, the SW-IMRT plans significantly reduced the dose to most SWOARs that differed according to tumor location, as shown in Table 2.

Assessment of dysphagia

Physician-reported dysphagia was significantly less frequent in the SW-IMRT group than in the ST-IMRT group during follow-up visits at 1,3, 6 months, and up to one-year

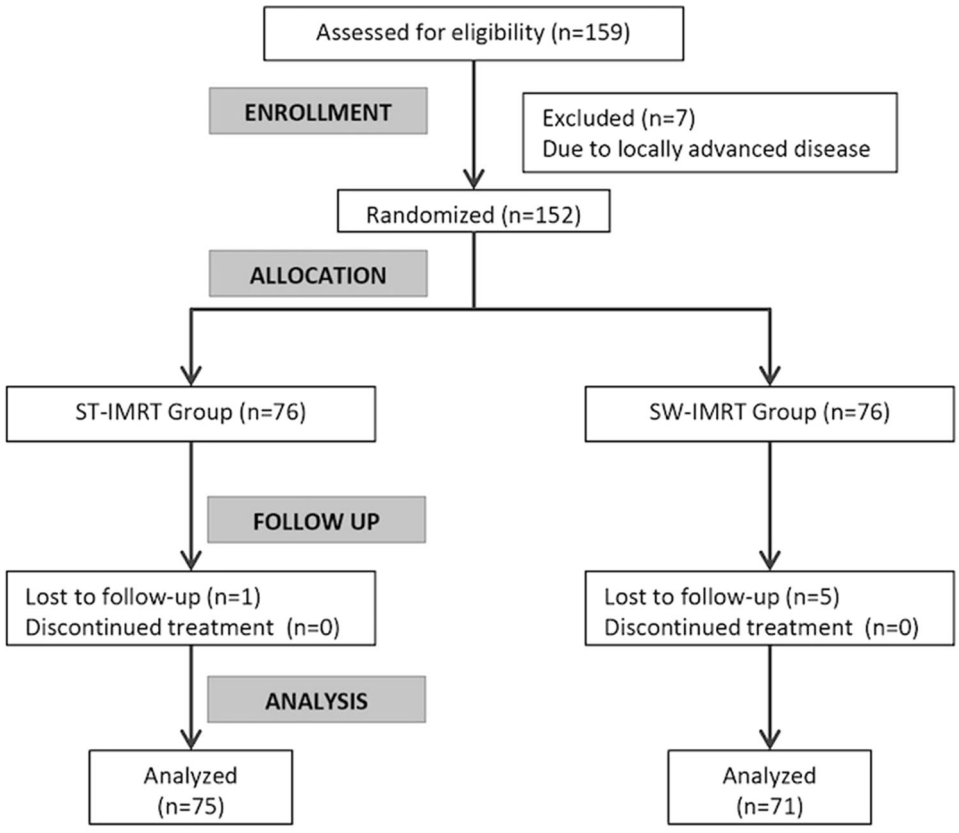

Figure 1. CONSORT diagram.

Table 1. Baseline characteristics of the two studied groups.

	SW-IMRT Group ($n = 71$)	ST-IMRT Group ($n = 75$)	p Value
Age (years)	49.6±11.7	52.6 ±13.4	0.160
Sex (male/female)	47/24	50/25	0.952
Performance status (0/1)	36/35	34/41	0.516
Primary site			0.254
Nasopharynx	24 (33.8%)	27 (36.0%)	
Larynx	16 (22.5%)	27 (36.0%)	
Oral cavity	16 (22.5%)	12 (16.0%)	
Hypopharynx	8 (11.3%)	6 (8.0%)	
Oropharynx	7 (9.9%)	3 (4.0%)	
T classification			0.736
T1	6 (8.5%)	7 (9.3%)	
T2	21 (29.6%)	26 (34.7%)	
T3	33 (46.5%)	28 (37.3%)	
T4	11 (15.5%)	14 (18.7%)	
N classification			0.932
N0	23 (32.4%)	27 (36.0%)	
N1	9 (12.7%)	7 (9.3%)	
N2	35 (49.3%)	37 (49.3%)	
N3	4 (5.6%)	4 (5.3%)	
Stage			0.978
I	2 (2.8%)	1 (1.3%)	
II	8 (11.3%)	8 (10.7%)	
III	31 (43.7%)	35 (46.7%)	
IV	30 (42.3%)	31 (41.3%)	
Treatment			0.455
Adjuvant	10 (14.1%)	14 (18.7%)	
Definitive	61 (85.9%)	61 (81.3%)	

Data are expressed as mean ± SD, or number (%).

postradiotherapy treatment. The two groups were comparable in dysphagia frequency during treatment. Using Videofluoroscopy (VF), dysphagia was significantly less common in the SW-IMRT group than the ST-IMRT group 3, 6, and 12 months after treatment (Table 3).

The relation between dysphagia at six months and dose to SWOARs

In patients with nasopharyngeal carcinoma, dysphagia developed after six months was significantly associated with higher doses delivered to SWOARs (Table 4). Similarly, patients with laryngeal and hypopharyngeal carcinoma who developed dysphagia at six months had significantly higher doses delivered to the base of the tongue (Table 4). We had only 10 patients with primary oropharyngeal carcinoma, so no analysis was done for this subgroup.

Development of dysphagia at six months was significantly more common in the ST-IMRT group than in the SW-IMRT group ($p < 0.001$). Also, it was more common in females ($p = 0.001$). Adjuvant RTH was associated with a higher proportion of dysphagia, with a near significant difference ($p = 0.083$) than radical RTH (Table 2 Supplementary data).

Factors associated with developing dysphagia with a p-value ≤ 0.1 on univariate analysis were entered in a logistic regression model. SW-IMRT was protective against developing dysphagia ($p < 0.001$), with an odds ratio (OR) of 0.14 (95%CI: 0.06–0.35). Besides, the female sex carried a 5.7-fold risk to develop dysphagia (Table 3 Supplementary data).

Survival analysis

The median follow-up period was 33 months. The overall survival (OS) of the whole group was 62.3%. Overall survival was not affected by RTH modality ($p = 0.811$). The OS of ST-IMRT group was 57.8%, and that of SW-IMRT group was 65.2%. The disease-free survival of the whole group was

Table 2. The mean dose (in Gy) delivered to SWOARs in patients with nasopharyngeal, laryngeal, and hypopharyngeal carcinomas in the two studied groups.

	SW-IMRT Group	ST-IMRT Group	*p* Value
Nasopharyngeal	***n* = 22**	***n* = 26**	
Base of tongue	40.7±7.2	55.7±7.3	<0.001
Inferior pharyngeal constrictor	51.9±5.3	56.4±6.4	0.012
Cricopharyngeus	51.7±4.4	54.7±6.5	0.081
Esophageal inlet	47.3±11.6	52.9±5.5	0.040
Cervical esophagus	43.6 ±9.0	45.3±5.4	0.466
Glottic larynx	45.8± 5.5	47.2± 6.1	0.410
Supraglottic larynx	48.8± 5.7	53.8±6.5	0.010
Laryngeal and hypopharyngeal	***n* = 22**	***n* = 27**	
Base of tongue	43.7± 8.0	55.2± 6.7	<0.001
Superior pharyngeal constrictor	42.3±7.8	41.0 ±9.4	0.640

Data are expressed as mean±SD.

Table 3. Assessment of dysphagia in the two studied groups during treatment and up to one year after treatment.

Dysphagia	SW-IMRT	ST-IMRT	*p* Value
During treatment			
G0	10 (14.1%)	7 (9.3%)	0.262
≥ G1	61 (85.9%)	68 (90.7%)	
n	71	75	
At 1 month			
G0	32 (48.5%)	13 (20.3%)	0.001
≥ G1	34 (51.5%)	51 (79.7%)	
*n**	66	64	
At 3 months			
G0	35 (55.6%)	14 (23.7%)	<0.001
≥ G1	28 (44.4%)	45 (76.3%)	
n	63	59	
At 6 months			
G0	38 (65.5%)	12 (22.2%)	<0.001
≥ G1	20 (34.5%)	42 (77.8%)	
n	58	54	
At 1 year			
G0	28 (59.6%)	13 (30.2%)	0.006
≥ G1	19 (40.4%)	30 (69.8%)	
n	47	43	
Videofluoroscopy (DIGEST)			
At 3 months			
0–1	26 (76.5%)	8 (36.4%)	0.005
2–4	8 (23.5%)	14 (63.6%)	
n	34	22	
At 6 months			
0–1	23 (82.1%)	9 (42.9%)	0.006
2–4	5 (17.9%)	12 (57.1%)	
n	28	21	
At > 1 year			
0–1	10 (76.9%)	3 (30.0%)	0.04
2–4	3 (23.1%)	7 (70.0%)	
n	13	10	

*The numbers examined are those available at the time of examination after dropping those patients who died or developed recurrence or distant metastases.
Data are expressed as number (%).

59.7%. Local control for ST-IMRT group was 81.2%, and SW-IMRT was 76.6% ($p = 0.470$). In general, there was no statistically significant difference in survival between treatment groups. (Figures 2a,b Supplementary data).

Discussion

After head and neck irradiation in HNC, dysphagia can affect the patient's physical, social, and emotional status. Around 50% of patients report dysphagia as a distressing symptom a year after treatment [11]. Finding efficient swallowing sparing

Table 4. The relation between the development of ≥ G1 dysphagia at six months and dose to SWOARs in nasopharyngeal, laryngeal, and hypopharyngeal carcinomas in the two studied groups.

	No dysphagia	≥ G1 dysphagia	*p* Value
Nasopharyngeal	***n* = 14**	***n* = 22**	
Base of tongue mean dose	44.1±10.3	52.0± 9.1	0.018
Base of tongue maximum dose	62.9± 6.2	68.7± 4.7	0.003
MPC mean dose	54.7±5.1	60.0± 6.4	0.013
MPC V55 (%)	45.2 (6.9–100.0)	100.0 (0.0–100.0)	0.014
MPC V60 (%)	18.4 (0.4–85.7)	84.9 (0.0–100.0)	0.004
MPC V65 (%)	0.0 (0.0–6.4)	6.3 (0.0–76.8)	0.003
IPC mean dose	51.8±4.3	56.4±6.6	0.027
IPC V55 (%)	22.4 (3.6–98.4)	91.2 (0.0–100.0)	0.012
IPC V60 (%)	1.9 (0.1–44.8)	34.6 (0.0–100.0)	0.027
IPC V65 (%)	0.0 (0.0–0.7)	0.0 (0.0–54.1)	0.484
Cricopharyngeus *m*. mean dose	51.7±3.8	55.6±6.1	0.047
Supraglottic larynx mean dose	48.9±5.3	54.4±6.4	0.012
Laryngeal and hypopharyngeal	***n* = 22**	***n* = 15**	
Base of tongue mean dose	47.6± 9.2	54.7± 7.3	0.019

Data are presented as mean±SD, or median (range).
MPC: middle pharyngeal constrictor muscle, IPC: interior pharyngeal constrictor muscle, V40: volume receiving 40 Gy, V50: volume receiving 50 Gy, V55: volume receiving 55 Gy.

radiotherapy techniques is essential because these health-related QOL measures influence curative management strategies [5].

Swallowing involves a sequence of coordinated events, including more than 30 pairs of muscles and six cranial nerves. It involves voluntary and involuntary stages. Patients can bypass the voluntary stage, but the involuntary stage must be triggered [12]. Radiation has a detrimental effect on the muscles involved in the swallowing process [13].

Many researchers have studied the dose–effect relationship between irradiated structures and dysphagia. The results of published studies on the critical structures related to swallowing dysfunction are identical. Most published studies explored a heterogeneous group of patients with limited consensus regarding the swallowing structure spared and contouring guidelines used. All studies agreed about the benefit following prospective sparing of swallowing structures.

Also, there is no consistency in how swallowing problems should be assessed, which remains one of the difficulties in understanding the literature in this area. We used two different assessment methods of dysphagia: physician-reported and objective assessment using VF. However, the lack of randomized controlled trials establishing the superiority of SW-IMRT over ST-IMRT in the era of evidence-based medicine calls into question the validity of any reported benefits and restricts its use in routine practice.

This mandates a prospective study design that several investigators proposed, as Van der Laan *et al.* [14]. A phase-III multicenter randomized controlled trial, the DARS trial [15], investigated the result of swallowing sparing strategies on pharyngeal cancer cases. The current study was designed to determine whether decreasing the dose to the SWOARS in patients with different HNCs with SW-IMRT will improve long-term swallowing dysfunction without any negative impact on survival.

Dutch radiation oncologists proposed the normal tissue complication probability (NTCP) model, developed by Dutch radiation oncologists, as a viable alternative to randomized

controlled trials. Any future benefit expected early in this multistep approach was verified later by validating model-based predictions in a prospectively followed up sample of patients [16].

Van Der Laan *et al.* performed a study to determine the possible benefits of SW-IMRT and the factors that influence those benefits. The doses to the SWOARs were reduced in the following order: SPC mean dose, supraglottic larynx mean dose, MPC mean dose, and proportion of EIM receiving less than 60 Gy. SW-IMRT dose reductions and absolute dose values varied by patient and SWOAR and depended on N stage and tumor site. The decline in expected RTOG G2-4 swallowing dysfunction was 9 percent on average. They concluded that the value of SW-IMRT is dependent on the amount of overlap between SWOARs and PTVs, neck RT, and tumor location [16].

Finally, in a cohort study of 186 patients who obtained SW-IMRT, their model was clinically confirmed. The SW-IMRT technique had no impact on the coverage of the target volume, which had been a significant flaw in previous studies [17].

They published the multivariable NTCP model for swallowing dysfunction at six months in patients treated with SW-IMRT; swallowing dysfunction is reduced by lowering the dose parameters used in the NTCP model. The high ΔNTCP group included patients with advanced T-stages and nasopharyngeal and oropharyngeal cancers. Those patients received higher doses to SPC and supraglottic larynx [17].

In our study, SW-IMRT is better than ST-IMRT regarding physician-reported dysphagia at 1, 3, 6 months, and one year with a statistically significant difference ($p = 0.001$, <0.001, <0.001, and 0.006, respectively). Objective assessment of swallowing using VF with DIGEST scale interpretation shows a statistically significant difference between groups at six months and one year. Development of dysphagia at six months was also more common in females and apparently more frequent in patients who received adjuvant radiotherapy compared to radical treatment. We did not find a significant difference between both techniques in physician-rated acute (during treatment) dysphagia using CTCAEv4 ($p > 0.05$). In the SW-IMRT group, 68 patients (90.7%) developed $\geq$ G1 dysphagia during treatment, compared to 61 patients (85.9%) in the ST-IMRT group ($p = 0.262$).

Eisbruch and colleagues demonstrated the clear effect of PCM, glottic, and SGL irradiation on persistent swallowing impairment after chemoradiotherapy in HNC [18]. They defined the pharyngeal constrictor muscles as one structure and found a significant relationship with mean dose, V50, V60, V65, the VF score, and the QOL questionnaire, and this was the same with Feng et al. [10,19]. They reported that 50 Gy was the lowest maximum dose given to a structure volume to reduce late dysphagia, which means minimizing the volumes receiving 50 Gy in those essential dysphagia-related structures can be clinically beneficial. In SWOARs, IMRT decreased V50 by 7-10% on average compared to 3 D conformal RT (3DCRT) [18].

Several trials were conducted to determine if reducing the dose to the SWOARS could improve swallowing outcomes in patients with HNC treated with IMRT. According to these results, increasing radiation to a larger PCM volume resulted in worse dysphagia [4].

> Dirix et al. reported that the mean dose and V50 to the IPC muscle and SGL were not associated with late dysphagia in univariate analysis but multivariate analysis [20]. Caudell et al. reported that a mean laryngeal dose greater than 41 Gy and V60 greater than 24% is strongly correlated with PEG tube dependency and aspiration. Increased PEG tube dependency and aspiration were also associated with V60 greater than 12% to the IPC. V65 ratio of more than 33% to the SPC or more than 75% to the MPC was correlated with pharyngoesophageal stricture needing dilation [21].

Using subjective scoring systems, Christianen et al. noticed several correlations between the mean dose to SWOARS and late swallowing dysfunctions. They first established that mean SPC and SGL doses were the most predictive of RTOG grade-2 dysphagia six months after the end of treatment in a heterogeneous group of patients [22].

We found a relation between dysphagia at six months and one year and the dose received to SWOARs that differs according to the tumor site. In nasopharyngeal cases, there was a statistically significant relation between physician-reported $\geq$ G1 dysphagia and MPC mean dose, V55, V60, V65, IPC mean dose, V55, V60, V65.

The Danish HNC study group (DAHANCA) reported that severe acute and late dysphagia rates might reach 38% and 14%, respectively, after radiotherapy treatment. Besides, tumor site, stage, and age are also associated with dysphagia [23,24].

According to Graff et al. [25], the risk of developing chronic dysphagia is mainly related to the PCM mean dose. To our knowledge, the cricopharyngeus muscle and base of the tongue were not reported before in dosimetric trials assessing crucial structures for late dysphagia.

There was a statistically significant relation between physician-reported $\geq$ G1 dysphagia and SGL mean dose, but regarding EIM, cervical esophagus, and glottic larynx, we didn't find any relation between those structures and dysphagia assessed at six months. Those results were in contrast to results reported by Feng et al. [10], Jensen et al. [26], Caglar et al. [27]. They found a significant relationship between glottis and supraglottic larynx and partial volumes of these structures. This discrepancy may be because our study included a mix of HNC subsites.

The studies by Werbrouck et al. [3] and Caglar et al. [27] included different HNC subsites and assessed acute dysphagia. Werbrouck et al. [3] had a study population of 88 IMRT treated HNC patients. Mucositis, dermatitis, and dysphagia were scored weekly during treatment. They had chosen the highest grade of toxicity as the reference value. Mucositis and dysphagia development were strongly related to the oral cavity and PCM mean dose.

Caglar et al. [27] evaluated 96 patients for early (1–2 months post-treatment) swallowing dysfunction after IMRT. The larynx and IPC mean dose highly correlated with aspiration ($p = 0.003$ and $p = 0.007$). A mean IPC dose of <54 Gy or a mean larynx dose of <48.2 was not associated with clinically significant aspiration. The IPC and cervical

esophagus mean dose correlated significantly with the development of strictures ($p = 0.02$ and $p = 0.04$). Mean IPC dose of < 54 Gy did not develop stricture. There were no strictures with any of the patients, and the IPC mean dose, V55, V60, V65, correlated with $\geq$ G1 dysphagia in our study.

Feng et al. [10] revealed that attempts to spare volumes of swallowing structures outside the PTV didn't affect locoregional control rates. We also found no significant difference between groups regarding local control and survival.

There were several limitations to the current study. That was a small sample size. In the same group, we looked at radical and adjuvant treated patients with various primary locations in the head and neck, and therefore different treated volumes. Not all patients underwent VF examination. These limitations, however, were similar to those seen in previous studies, and the lack of results published from prospective randomized trials limited that comparison with other results.

Conclusion

Our study found that SW-IMRT is significantly better than ST-IMRT regarding the physician-rated and objective assessment of swallowing dysfunction at one, three, six months, and one-year post-treatment. However, these data showed heterogeneity in the treatment site in both groups. We are waiting for longer follow-up results on a larger number of patients.

Disclosure statement

The authors report no conflicts of interest.

Funding

The authors received no financial support for the research.

ORCID

May Gamal Ashour http://orcid.org/0000-0002-9495-5937
Reem Emad El Din http://orcid.org/0000-0003-3457-8735
Mohammed Mohammed Gomaa http://orcid.org/0000-0003-1670-8532
Shaimaa Abdelgeleel http://orcid.org/0000-0003-0994-7703

References

[1] Kim DR, Duprez F, Werbrouck J, et al. A predictive model for dysphagia following IMRT for head and neck cancer: Introduction of the EMLasso technique. Radiother Oncol. 2013;107(3):295–299.
[2] Murphy BA. Late treatment effects: reframing the questions. Lancet Oncol. 2009;10(6):530–531.
[3] Werbrouck J, De Ruyck K, Duprez F, et al. Acute normal tissue reactions in head-and-Neck cancer patients treated with IMRT: Influence of dose and association with genetic polymorphisms in DNA DSB repair genes. Int J Radiat Oncol Biol Phys. 2009;73(4):1187–1195.
[4] Wang X, Eisbruch A. IMRT for head and neck cancer: reducing xerostomia and dysphagia. J Radiat Res. 2016;57(S1):i69–i75.
[5] Petkar I, Bhide S, Newbold K, et al. Dysphagia-optimised intensity-modulated radiotherapy techniques in pharyngeal cancers: is anyone going to swallow it? Clin Oncol (R Coll Radiol). 2017;29(7):e110–e118.
[6] Christianen MEMC, Langendijk JA, Westerlaan HE, et al. Delineation of organs at risk involved in swallowing for radiotherapy treatment planning. Radiother Oncol. 2011;101(3):394–402.
[7] National Cancer Institute. Common Terminology Criteria for Adverse Events v.4.0 (CTCAE). Available from: http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm.
[8] Cox JD, Stetz J, Pajak TF. Toxicity criteria of the radiation therapy oncology group (RTOG) and the european organization for research and treatment of cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995;31(5):1341–1346.
[9] Hutcheson KA, Barrow MP, Barringer DA, et al. Dynamic imaging grade of swallowing toxicity (DIGEST): scale development and validation. Cancer. 2017;123(1):62–70. 2016/08/26.
[10] Feng FY, Kim HM, Lyden TH, et al. Intensity-modulated chemoradiotherapy aiming to reduce dysphagia in patients with oropharyngeal cancer: clinical and functional results. J Clin Oncol. 2010;28(16):2732–2738.
[11] Roe JWG, Drinnan MJ, Carding PN, et al. Patient-reported outcomes following parotid-sparing intensity-modulated radiotherapy for head and neck cancer. How important is dysphagia? Oral Oncol. 2014;50(12):1182–1187.
[12] Rosenthal DI, Lewin JS, Eisbruch A. Prevention and treatment of dysphagia and aspiration after chemoradiation for head and neck cancer. J Clin Oncol. 2006;24(17):2636–2643.
[13] Popovtzer A, Cao Y, Feng FY, et al. Anatomical changes in the pharyngeal constrictors after chemo-irradiation of head and neck cancer and their dose–effect relationships: MRI-based study. Radiother Oncol. 2009;93(3):510–515.
[14] Van Der Laan HP, Christianen MEMC, Bijl HP, et al. The potential benefit of swallowing sparing intensity modulated radiotherapy to reduce swallowing dysfunction: an in silico planning comparative study. Radiother Oncol. 2012;103(1):76–81.
[15] Petkar I, Rooney K, Roe JWG, et al. DARS: a phase III randomised multicentre study of dysphagia- optimised intensity modulated radiotherapy (Do-IMRT) versus standard intensity- modulated radiotherapy (S-IMRT) in head and neck cancer. BMC Cancer. 2016;16(1):1–10.
[16] Van Der Laan HP, Gawryszuk A, Christianen MEMC, et al. Swallowing-sparing intensity-modulated radiotherapy for head and neck cancer patients: treatment planning optimization and clinical introduction. Radiother Oncol. 2013;107(3):282–287.
[17] Christianen MEMC, Van Der Schaaf A, Van Der Laan HP, et al. Swallowing sparing intensity modulated radiotherapy (SW-IMRT) in head and neck cancer: clinical validation according to the model-based approach. Radiother Oncol. 2016;118(2):298–303.
[18] Eisbruch A, Schwartz M, Rasch C, et al. Dysphagia and aspiration after chemoradiotherapy for head-and-neck cancer: which anatomic structures are affected and can they be spared by IMRT? Int J Radiat Oncol Biol Phys. 2004;60(5):1425–1439.
[19] Feng FY, Kim HM, Lyden TH, et al. Intensity-Modulated radiotherapy of head and neck cancer aiming to reduce dysphagia: early dose-effect relationships for the swallowing structures. Int J Radiat Oncol Biol Phys. 2007;68(5):1289–1298.
[20] Dirix P, Abbeel S, Vanstraelen B, et al. Dysphagia after chemoradiotherapy for head-and-Neck squamous cell carcinoma: Dose-Effect relationships for the swallowing structures. Int J Radiat Oncol Biol Phys. 2009;75(2):385–392.
[21] Caudell JJ, Burnett OL, Schaner PE, et al. Comparison of methods to reduce dose to swallowing-related structures in head and neck cancer. Int J Radiat Oncol Biol Phys. 2010;77(2):462–467.
[22] Christianen MEMC, Schilstra C, Beetz I, et al. Predictive modelling for swallowing dysfunction after primary (chemo)radiation: results

of a prospective observational study. Radiother Oncol. 2012; 105(1):107–114.

[23] Mortensen HR, Overgaard J, Jensen K, et al. Factors associated with acute and late dysphagia in the DAHANCA 6 & 7 randomized trial with accelerated radiotherapy for head and neck cancer. Acta Oncol. 2013;52(7):1535–1542.

[24] Mortensen HR, Jensen K, Aksglaede K, et al. Late dysphagia after IMRT for head and neck cancer and correlation with dose-volume parameters. Radiother Oncol. 2013;107(3):288–294.

[25] Graff P, Woisard V, Racadot S, et al. Radiothérapie conformationnelle avec modulation d'intensité des cancers des voies aérodigestives supérieures: dose de tolérance des tissus sains. Muscles constricteurs du pharynx et larynx. Cancer/Radiothérapie. 2016;20(6-7):452–458.

[26] Jensen K, Lambertsen K, Grau C. Late swallowing dysfunction and dysphagia after radiotherapy for pharynx cancer: frequency, intensity and correlation with dose and volume parameters. Radiother Oncol. 2007;85(1):74–82.

[27] Caglar HB, Tishler RB, Othus M, et al. Dose to larynx predicts for swallowing complications after intensity-modulated radiotherapy. Int J Radiat Oncol Biol Phys. 2008;72(4): 1110–1118.