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Research Article

Dysphagia Aspiration Related Structures [DARS] Optimised Volumetric Modulated Arc Therapy in Head and Neck Cancers

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Abstract

Background and purpose: There is a significant relationship between radiation dose to the pharyngeal constrictor muscles (PCM) and swallowing dysfunction during chemoradiotherapy of head and neck cancers. We aimed at sparing the pharyngeal constrictors using VMAT and assessing its impact on swallowing function.

Materials and methods: 28 patients with squamous cell carcinoma of oropharynx, hypopharynx, larynx and oral cavity, received a dose of 66Gy in 30 fractions. Doses to the constrictor muscles were constrained. The primary endpoint was the difference in the mean MD Anderson dysphagia inventory (MDADI) composite scores, at baseline and 3 months post radiotherapy. Objective assessments were done using Functional Endoscopic Evaluation of Swallowing (FEES).

Results: The Superior, Middle and inferior constrictor out received a mean dose of 43.5 Gy (SD 9.6), 48.6 Gy (SD 4.5) and 24.2 Gy (SD 11.1) respectively. We found a statistically significant between group difference of 14.2 + 6.1 in the mean MDADI composite scores between the two groups. 40% of the patients were grade 1on Murray`s secretion scale pre-treatment vs 15% at 3 months post treatment. During pre-treatment assessment by FEES, 14% of the patients were classified as penetrators and none were aspirators as per the Rosenbek's Penetration-Aspiration scale vs 10.7% penetrators and no aspirators at 3 months post treatment.

Conclusion: DARS optimised radiotherapy with SIB-VMAT is feasible in patients with head and neck cancers and has potential to decrease the severity of dysphagia without compromising the overall treatment outcomes.

INTRODUCTION

According to the Globocan statistics for 2020, head and neck cancer accounts for more than 870,000 cases and 440,000 worldwide deaths annually [1]. More than 70% of patients with head and neck cancer (HNC) need radiation in the definitive, adjuvant, or palliative settings. Radiation is however associated with long-term toxicities such as xerostomia and swallowing dysfunction. Both xerostomia and swallowing dysfunction lead to late dysphagia, which has been reported in around 50 % of the patients [2].

The structures related to the swallowing mechanism are the pharyngeal constrictor muscles (PCM). Since the swallowing structures are adjacent to the tumor, sparing these structures is quite challenging without compromising the tumor dose.There is a significant relationship between the radiation doses to the PCM and swallowing dysfunction [3]. Popovzter et al., compared the MRI finding in 12 patients with stage III–IV head and neck cancer before and 3 months after completing chemo-irradiation. They found that T1-weighted signals decreased and the T2-weighted signals increased in the pharyngeal constrictor muscle which received >50 Gy [4]. In the CRUK/14/014 trial, dysphagia optimized IMRT reduced the dose to swallowing structures and improved the swallowing function assessed subjectively by MD Anderson dysphagia inventory [MDADI] scores [5].

Both subjective and objective tests are used to evaluate swallowing outcome measures. The two common instrumental methods (objective tests) which are available to determine and quantify functional abnormalities in swallowing and the risk to aspirate are video fluoroscopy (VF) and Fiberoptic Endoscopic Evaluation of Swallowing (FEES) [6]. Eisbruch et al., assessed the dosimetric correlates of long-term dysphagia assessed by VF

after concurrent chemo-intensity-modulated radiotherapy. For increased VF-based aspirations scores, TD50 and TD25 were 63 Gy and 56 Gy for pharyngeal constrictors, and 56 Gy and 39 Gy for supraglottic larynx, respectively [7].

Subjective evaluation of dysphagia is achieved using various physician and patient reported questionnaires.The MDADI composite score is a validated patient reported swallowing specific questionnaire and has been adopted as a tool to assess the swallowing functional outcome in head and neck cancer trials [8]. Hutcheson et al., conducted a retrospective cross-sectional study in 1,136 HNC patients. They identified that a 10-point between-group difference in composite MDADI scores was associated with clinically meaningful difference in swallowing function [9].

Studies reporting on the post-treatment functional status assessed objectively by FEES after DARS sparing is rare. The aim of this study was to assess the feasibility of simultaneous integrated boost, volumetric modulated arc therapy (SIB_VMAT) in sparing DARS and its impact on functional outcome assessed subjectively by the MDADI score and objectively by FEES.

MATERIALS AND METHODS

Patient selection

The patient recruitment for the study was started between Feb 2018 to Aug 2019. Patients in the age group of 18 and 65 years and WHO performance status 0,1 or 2 with biopsy proven squamous cell carcinoma of the oropharynx, larynx, hypopharynx and oral cavity (stage T1-4, N0-3, M0) were included in the study. Convenience sampling was used to select patients. Patients with pre-existing swallowing dysfunction not related to head and neck cancer, previous radiotherapy to the head and neck region, posterior pharyngeal wall, post- cricoid and retropharyngeal lymph node involvement, well lateralized tumors requiring unilateral irradiation, major head and neck surgery in the past, and tracheostomized patients were excluded from the study. A written informed consent was obtained from the participants. The study was done in accordance with Good Clinical Practice Guidelines and the Declaration of Helsinki and was approved by our institutional ethics committee on March 8, 2017.

Patient evaluation and assessment of dysphagia

Hemogram and baseline biochemical investigations were done at enrollment for all patients. All patients underwent contrast enhanced computed tomography (CECT) of the neck at baseline and 3 months after completion of treatment. Subjective evaluation was done using the MDADI questionnaire which quantifies an individual`s global, physical, emotional and functional perceptions of swallowing ability. It is a self administered patient response outcome (PRO) questionnaire which was used to obtain the global and composite MDADI scores before treatment and 3 months after completion of radiation.A 10-point between-group difference in composite MDADI scores was associated with clinically meaningful difference in swallowing function [9].

FEES was done using a 4mm flexible nasal endoscope and digital recording in the operation theatre after taking informed consent. The endoscopy was done twice; pre-treatment and 3 months after completion of treatment. The evaluation was done by ENT surgeons. The pretreatment and post treatment evaluation was done by different ENT surgeons in order to reduce assessment bias.For static evaluation, the tip of the endoscope was placed at three main positions: naos-pharyngeal; velum palate (it is possible to detect stagnation of secretions in the glosso-epiglottic vallecula, the pyriform recesses, the inter arytenoids area and the laryngeal vestibule) and thirdly with the endoscope placed at the laryngeal aditus. The laryngeal sphincter function was tested by simply inviting the patient to cough, swallow saliva and carry out a valsalva manoeuvre and was rated by the Murray Secretion Rating (MSS) (Table 1). For dynamic evaluation, patients were asked to drink 10 mL of blue dyed water and were rated by using Rosenbek's Penetration-Aspiration scale. The scale ranges from 1 (material does not enter the airway) to 8 (material enters the airway, passes below the vocal folds, and no effort is made to eject). If the patient passed evaluation II successfully, (Scale 1 by Rosenback), then the patient was administered with 5 ml yoghurt to continue the dynamic test. The end was the measurement by Pharyngeal Residue Severity Scale (0-4) (Table 1 and 2).

Planning and Target volume delineation

Pre-therapy CECT and findings at the time of endoscopy were used for accurate delineation of the gross tumor. Three clinical

Table 1: Murray Secretion Rating (evaluation 1)

0	Normal rating: ranges from no visible secretions anywhere in the hypopharynx, to some transient secretions visible in the valleculae and pyriform sinuses. These secretions are not bilateral or deeply pooled.
1	Any secretions evident upon entry or following a dry swallow in the protective structures surrounding the laryngeal vestibule that are bilaterally represented or deeply pooled.
2	Any secretions that change from "1" to a "3" rating during the observation period.
3	Most severe rating. Any secretions seen in the area defined as laryngeal vestibule. Pulmonary secretions are included if they are not cleared by swallowing or coughing by the closing of the segment.

Table 2 - Demography, baseline and treatment characteristics

Mean age	56 years (SD 7.81)
Males	22 (78.5%)
Females	6 (21.5%)
Smokers	20 (71.4%)
Comorbidities	10 (35.7%)
Tumour site Oral cavity Oropharynx Supraglottis Glottis Hypopharynx	 11 (39.2%) 9 (32.3%) 6 (21.5%) 1 (3.5%) 1 (3.5%)
Stage I II III IV	 4 (14.3%) 4 (14.3%) 6 (21.4%) 14 (50%)
Concurrent Cisplatin Yes No	 27 (96.4%) 1 (3.2%)

target volumes (CTV) were delineated. CTV_6600 included the primary and nodal gross tumor volume (GTV) with a 1 cm isotropic margin, CTV_6000 volume included the nodal levels at risk in close proximity to the involved nodal station and the remainder of the uninvolved primary site at risk for microscopic spread, CTV_5400 included the remaining nodal levels at risk of microscopic disease. Corresponding planning target volumes (PTVs) were expanded with 5 mm margins. All PTVs were restricted to 5 mm within the skin surface for the purpose of dose optimization and evaluation. CT delineation of nodal levels was followed by the recently updated outlining guidelines [10,11].

The superior, middle and inferior pharyngeal constrictors were contoured and delineated as separate structures. Outlining for the PCM was based on the published contouring guidelines defined by Christianen et al., in conjunction with the atlas produced for the Post-operative adjuvant treatment for HPV positive tumors (PATHOS; NCT02215265) trial [12,13].

We based our OAR constraints on the RCT by Petkar et al [14,l5]. For oropharyngeal primaries, mean dose constraints of <50 Gy to the volume of superior and middle pharyngeal constrictor muscles (SMPCM) lying outside PTV_6600 (Plan-SMPCM), and <20 Gy to the volume of inferior pharyngeal constrictors (IPCM) lying outside PTV_6600 (Plan-IPCM) were defined [5]. For hypopharyngeal tumors, optimal mean dose constraints of <50 Gy and <40 Gy were set for Plan-SMPCM and Plan-IPCM respectively.

Priority was given to the PTV coverage. The constrictor muscles that lay within the PTV_6600 were not spared. The criteria of at least 98% of each PTV being covered with 95% of the prescribed dose (PTV_V95 > 98%) and the volume receiving 7062cGy (107%) not exceeding 2 cm^3 was followed. All patients received 66Gy in 30 fractions to PTV_6600, 60Gy in 30 fractions to PTV_6000 and 54Gy in 30 fractions to PTV_5400 using a 6X photon beam with SIB-VMAT technique. A patient specific quality assurance check was performed for all approved treatment plans using the Varian Clinac iX treatment unit and Electronic Portal Imaging Device (EPID). All plans were passed for treatment with 3mm distance to agreement (DTA) and 3% dose difference (DD) criteria.

VMAT planning

Multiple plans for DARS sparing were performed to achieve the specific constraints. DARS plans were iterated utilizing the Varian Eclipse Planning system version. 10.0, with Anisotropic Analytical Algorithm (AAA) and 6x photon beam with a dose rate of 600MU/min for Varian Clinac iX. For each plan, depending on the site VMAT was delivered with two or four complete arcs. The gantry angle of rotation for the first arc started from 181° to 179°with collimation of 330° in the clockwise direction. The angle of rotation for the second arc started from 179° to 181° with collimation of 30° in counterclockwise directions. When constraints were not met, two more non- coplanar arcs were used, the third arc from 181° to 179° with collimation of 340° and couch 350° and the fourth arc from 179° to 181° with collimation of 20° and couch 10°. Treatment plans approved for treatment are verified using Electronic Portal Imaging Device (EPID). Patient-Specific Quality assurance was performed to assess the gamma pass criteria of 3mm (DTA) and 3% (DD) for global and local normalization. Gamma pass rates of more than 95% were used for testing.

Image guidance during radiation

Imaging protocol followed during radiation included Cone Beam computed tomography (CBCT) on days 1, 2 and 3 of treatment and then weekly after every 5 fractions of radiation.

Details of concurrent chemotherapy

Concomitant chemotherapy with Inj cisplatin 100 mg/m2 was administered on day 1, day 22 and day 42 of the radiotherapy schedule for all patients, unless there was a contraindication and creatinine clearance was less than 45ml/min.

Assessments

NCI CTCAE v5.0 used to assess acute toxicity and data was collected weekly during radiotherapy and at week 4 and 8 after treatment completion. Late toxicity was scored using both NCI CTCAE v5.0 and LENT SOMA scoring systems. Clinical assessments were made at 6 weeks and 3 months after completion of treatment. CECT was used for response assessment post 3 months after radiotherapy and was reported as per RECIST criteria.v1.1. Patients found to have residual tumor at the end of 3 months underwent salvage surgery if feasible. If the patient was not suitable for salvage surgery then palliative chemotherapy or best supportive care was planned. Late toxicity data was collected at 3 months post- treatment.

Statistical analysis

The statistical analysis was performed with IBM Statistical Package for the Social Sciences (SPSS) version 21 to interpret the results. The intrarater and interrater reliability for functional endoscopy assessments was assessed using the Kappa coefficient. The mean difference between pre-treatment and post-treatment functional endoscopy scores were performed using the paired t test. The comparison of MDADI scores before and after radiation was performed using the paired t-test. With significance of 0.05, power of 90%, drop rate of 30%, sample size calculated was 33.(Calculated using nMaster version 2.0; paired t test)

RESULTS

56 patients of head and neck cancer were assessed for eligibility, 14 patients did not meet the inclusion criteria and two patients were not willing to participate in the study. 40 patients were included in the study of which 6 patients chose to get treated elsewhere. 34 patients were started on treatment and 2 patients defaulted during the course of radiotherapy due to personal reasons. 32 patients completed the full course of treatment and 4 patients were lost to follow up post completion

of treatment. Out of the 28 patients included for the final analysis, 22 (78.5%) were males and 6 (21.5%) were females. The mean age was 56 (SD 7.81) years. 67% of the population were smokers. The patient and tumour characteristics are given in Table 2.

Out of the 28 patients, 11 had tumours of the oral cavity, 9 were oropharyngeal tumours, 6 were supraglottic tumours, 1 Glottic and hypo-pharyngeal tumour each. The histology was squamous cell carcinoma in all the cases. The majority of the cases were Stage IVA (50%) followed by stage III (23%) and stage II (14%). 27 (96.4%) out of the 28 patients received concurrent Cisplatin at 100 mg/m2 at 3 weekly intervals.

The dosimetric details of the PTVs and organs at risk are shown in Table 3. When the constrictors formed part of the PTV, the PTV was given priority so that the dose to the tumour was not compromised. 85% of the cases had a PTV involving at least some part of the constrictor volume. Separate structures of Sup cons_out, Mid cons_out and Inf cons_out were created using the volumes of respective constrictors lying outside the PTV and dose constraints were given for the same.

The 50Gy and 19.5Gy dose colour wash showing the sparing of superior and inferior constrictor muscles is shown in Figure 1 (a and b respectively).

The mean V50Gy for SMPCM was 77.1 % (SD 23.1) while the mean V40Gy for IPCM was 40.4% (SD 39.75%). The mean V50 for SMPCM were 74.85%, 83.79, 77.49%, 63.37% in oral cavity, oropharynx, supraglottic and glottic tumours respectively. The mean V40Gy for IPCM were 16.91%, 25.67%, 93.55%, 100% for oral cavity, oropharynx, supraglottic and glottic tumours respectively. Table 4 shows the site-wise distribution of achieved doses of constrictors.

Objective assessment of functional outcomes

FEES was done by a 3 staged evaluation, pre treatment and at 3 months post treatment. As per the MSS scale, MSS 2 and above are strongly correlated to an increased risk of aspiration. In our study, in the pretreatment evaluation none of the cases reached a score of 2 or above. 60% of the patients (n= 18) were rated MSS 0 and 40% (n= 10) were rated MSS 1 in the pre treatment setup. At 3 months post treatment 85% (n= 23) of the patients were rated MSS 0 and 15% (n=5) were rated MSS 1(p = 0.009) (Table 3).

In the Rosenbeck`s Penetration aspiration scale, scores 2 to 5 were classified as penetrators while 6 and above were classified as aspirators. in the pre-treatment evaluation there were 4 (14.2%) penetrators (3 in oral cavity tumours and 1 in Oropharynx) and no aspirators. At 3 months post treatment there were 3 patients (10.7%) in the penetration group (1 in oral cavity and 2 in oropharynx) and no aspirators (Table 5).

Subjective assessment of functional outcomes

The MDADI mean scores were calculated at baseline (pre treatment) and 3 months post treatment using the MDADI

Table 3: Dosimetry of PTVs and OARs

Site	PTV_HR D_mean Gy (SD)	PTV_IR D_mean Gy (SD)	PTV_LR D_mean Gy (SD)	LarynxD_mean Gy (SD)	Parotid_RT D_mean Gy (SD)	Parotid_LT D_mean Gy (SD)	Spinal cord D_max Gy (SD)
Oral cavity	66.16 (2.09)	66.33 (2.32)	65 (3.42)	48.21 (11.1)	34.68 (11.25)	36.15 (12.57)	45.05 (1.58)
Oropharynx	68 (1.24)	66.21 (1.52)	65.63 (1.24)	46.7 (8.57)	27.21 (4.57)	33.22 (16.25)	44.67 (2.56)
Hypopharynx	67.25	63.42	-	66.83	6.66	7.32	43.86
Supraglottis	67.14 (0.46)	63.88 (2.92)	62.79 (0.75)	65.74 (2.34)	23.73 (1.77)	23.91 (2.44)	45 (1.34)
Glottis	66.85	62.12		66.52	20.6	22.32	44.65

Table 4: Depicting the site wise distribution of achieved doses to the constrictors

SITE	MEAN DOSE (Gy) with SD								
	Sup cons	Sup cons_out	Mid cons	Mid cons_out	Inf cons	Inf cons_out	Total cons	Total cons_out	Larynx
Oral cavity (n=11)	58.5 (8.29)	48.4 (8.02)	56.27 (8.61)	47.15 (6.97)	30.18 (15.04)	21.34 (3.23)	48.32 (16.91)	35.66 (14.5)	48.2 (11.18)
Oropharynx (n=9)	62.08 (8.77)	45.33 (10.83)	61.5 (6.15)	49.57 (1.62)	30.09 (16.3)	31.3 (20.15)	51.22 (18.7)	43.86 (12.86)	46.71 (8.57)
Hypopharynx (n=1)	28.78	-	66.56	49.46	65.94	-	53.76	-	66.83
Supraglottis (n=6)	45.99 (6.6)	35.39 (4.03)	66.78 (0.82)	-	62.72 (7.3)		58.5 (10.7)		65.74 (2.35)
Glottis (n=1)	31.06	-	62.44	49.25	66	-	53.16		66.52
Total (n=28)	54.93 (11.95)	43.47 (9.6)	60.79 (7.52)	48.57 (4.46)	39.68 (20.24)	24.19 (11.08)	51.8 (16.68)	39.36 (13.38)	52.8 (11.89)

Table 5: Depicting the mean MDADI scores pre-treatment and 3 months post treatment

Site	Pre-treatment Mean (SD)		3 months post treatment Mean (SD)	
	Global score	Composite score	Global score	Composite score
Oral cavity (n=11)	3.09 (0.83)	58.45 (4.65)	3.36 (0.80)	71.27 (6.79)
Oropharynx (n=9)	2.11 (0.6)	56.55 (7.76)	2.77 (0.83)	71 (8.29)
Hypopharynx (n=1)	2	68	3	74
Supraglottis (n=6)	2.16 (0.75)	63.83 (4.44)	4.16 (0.75)	82.16 (3.25)
Glottis (n=1)	2	58	3	69
Total (n=28)	2.5 (0.83)	59.32 (6.30)	3.32 (0.9)	73.53 (7.8)

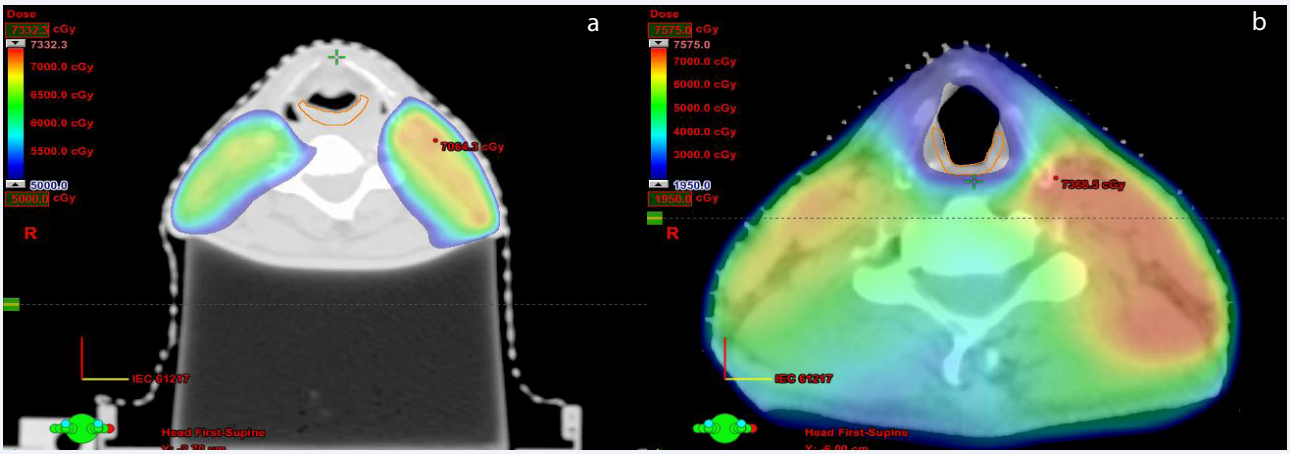

Figure 1 Showing the dose colour wash and spared middle and inferior constrictor muscles. a - 50 Gy dose colour wash showing the sparing of middle constrictor. b - 19.5 Gy dose colour wash showing the sparing of inferior constrictor

questionnaire. Each assessment gave 2 scores viz Global score and a Composite score. The mean global scores and composite scores pre-treatment and 3 months post treatment are shown in Table 5. There was a difference of 14.21 (SD 4.53) between the pre-treatment and 3 months post treatment composite MDADI scores ($p<0.001$)

Acute toxicities were graded based on RTOG grading. 57% developed grade 1 oral mucositis while 14.5% of the patients developed grade 2 oral mucositis while none developed grade 3 oral mucositis. 14.2 % patients developed grade 1 laryngitis, 7.3% developed grade 2 laryngitis and none had grade 3 laryngitis. Response assessment at the end of 3 months showed a complete response of 71%, partial response of 17.8% and stable disease in 10.2 % of the patients.

DISCUSSION

Studies reporting on the post-treatment functional status after DARS sparing is rare. We aimed to study the feasibility of SIB-VMAT in sparing DARS and its impact on functional outcome assessed subjectively by MDADI score and objectively by functional endoscopy. Since the pharyngeal constrictors are adjacent to the tumor, sparing these structures is quite challenging without compromising the tumor dose. We employed different optimisation constraints for the constrictors for the various subsites in head and neck malignancies.We used the optimisation constraints based on the ongoing RCT by Petkar et al in our study [14].

In our study in 85% of the cases, the high risk PTV_6600 overlapped with the constrictors. We decided that we would not spare the constrictors that lay within the high risk PTV. Hence we applied these dose constraints to the constrictors-out which was the volume of the constrictors lying outside the high risk PTV. For oral cavity and oropharyngeal primaries, mean dose constraints of <50 Gy to the volume of SMPCM lying outside the PTV_6600 and less than 20 Gy to the volume of IPCM lying outside PTV_6600 were defined."For laryngeal and hypopharyngeal tumors, mean dose constraints of <50 Gy and<40 Gy were used for SMPCM and IPCM respectively."

We were able to achieve sparing of the constrictors in our study. The Superior constrictor_out received a mean dose of 43.5 Gy (SD 9.6), Middle constrictor_out received a Dmean 48.6 Gy (SD 4.5) and in inferior constrictor_out the Dmean was 24.2 Gy (SD 11.1). In the CRUK/14/014 trial, the median doses received by the superior & middle PCM dose in the dysphagia optimised IMRT arm (Do-IMRT) was 49.7Gy (IQR 49.4 - 49.9), while inferior PCM doses were 28.4Gy (IQR: 21.3–37.4) in the Do-IMRT arm.

The degree to which DARS can be spared is site specific as seen from the results. Achieving a dose constraint of Dmean < 20 Gy to the inferior constrictors without compromising on the PTV dosage is more likely when the primary is in the oral cavity or select oropharynx. In our study in the oral cavity the mean dose to the inferior constrictors was 21.34 (SD 3.23). In oropharyngeal tumours it was 31.3 (SD 20.15). Similarly for the superior and middle constrictors the mean doses were 58.5 (SD 8.29) and 56.27 (SD 8.61) in the oral cavity respectively while in the oropharyngeal tumours the mean doses were superior constrictor 62.08 (SD 8.77) and middle constrictor 61.5 (SD 6.12). There was no volume of middle or inferior constrictor outside the PTV in supraglottic and hypopharyngeal tumours (Table 6).

In the study by Caglar HB et al., V55 < 80% and V65 < 30% for high superior pharyngeal constrictors were identified by univariate and multivariate analyses as predictors of swallowing dysfunction [15]. In our study V55 was 63.5% and V65 was 41%. In the study by Roe JWG et al "mean doses to the middle constrictors were predictive of acute dysphagia. An increased risk for the development of acute dysphagia was observed when constraints of mean dose (Dmean) <50Gy, maximum dose (D-max) <60Gy and V50Gy<70% were not met for MCM [16]. In our study for the MCM the D-mean was 48.6 Gy (SD 4.5), mean D-max was 62.4 Gy (SD 7.6) and mean V50 was 82.4% (SD 22.3).

In the study by Vlaich et al., maintaining the mean inferior constrictor dose to < 41 Gy and V40 to <41% helped to minimize gastrostomy tube dependence.[17] We achieved mean inferior constrictors dose of 39.7 Gy (SD 20.2) and V40 of 40.5%. None of our patients required gastrostomy post treatment.

In a study by Caglar et al., volume of the larynx receiving > 50Gy and volume of the inferior constrictor receiving >50Gy were significantly associated with both aspiration and strictures [13]. In our study mean dose to the larynx was 52.8 Gy (SD 11.9). We intentionally did not give constraints to the larynx inorder to avoid underdosing the tumour. Feng et al. evaluated the efficacy of swallow- sparing chemo-IMRT in 73 patients with stage III/IV oropharyngeal cancers [18]. Mean doses of 48 Gy and 42 Gy were achieved for the spared parts of PCM and supraglottic larynx respectively. In their study no relapses were observed within or near the spared structures and the long-term swallowing outcomes were only slightly worse compared to the baseline.

We assessed the impact of sparing the DARS on swallowing function by both subjective and objective assessments. We used MDADI scores for subjective assessment of dysphagia. MDADI scores have been used for reporting swallowing dysfunction in more than 40 publications. It has been validated in 5 languages and is the principal measure of swallowing related quality of life assessment.[8]

In our study DARS sparing resulted in an improvement in the composite MDADI scores at 3 months post-treatment indicating an improvement in swallowing function. Hutcheson et al identified a 10 point difference in the composite MDADI scores between the groups was associated with a clinically significant improvement in swallowing function [9]. We found a between group difference of 14.2 + 6.11; [95% CI:11.85-16.58 p < 0.001] in the mean MDADI composite scores between the pre-treatment and post-treatment group which was statistically significant. There was also a significant correlation between the middle constrictor (OUT) (rs= - 0.72, p= 0.002) and inferior constrictor (OUT) mean doses (rs= - o.47, p=0.048) with the post treatment MDADI scores at 3 months.

We used FEES for objective assessment of swallowing function. The subjective improvement in swallowing function in our study was confirmed by functional endoscopy. Chia-Wei kuo et al evaluated the ability of Murray secretion scale (MSS) in predicting the risk of aspiration and concluded that there was a linear correlation between MSS and the Penetration aspiration scale (PAS). Murrays secretion scale 2 (any secretions in the laryngeal vestibule in the observation period) and had a sensitivity and specificity of 74% and 90% respectively in relation to the PAS [19].

In our study 40% of the patients were rated grade 1 as per MSS pre treatment. None of the patients were MSS grade 2 or 3. At 3 months post treatment the proportion of the patients rated MSS grade-1 had decreased to 15%. Sparing the constrictors improved the swallowing function which was reflected objectively in the difference in the Murray scores (p=0.009)

Aspiration was also quantified using the validated 8-point penetration aspiration scale (PAS) developed by Rosenbeck [20]. Penetration was defined as passage of material into the larynx which does not pass below the vocal folds."Aspiration was defined as "passage of material below the level of the vocal folds." Aspiration is known to be more severe than penetration. Hence, aspiration was scored 6, 7, or 8. Penetration was scored either 2 or 3 if residue remains above the vocal folds and 4 or 5 if residue courses to the level of the vocal folds.

In our study during pre-treatment assessment by FEES, 14% of the patients were classified as penetrators and none were aspirators. At 3 months post treatment there was penetration in only 10.7% of the patients with one patient worsening from grade 2 to grade 3. We had no aspirators post treatment.

Our study has a few limitations. We objectively assessed the swallowing function 3 months post treatment. In the studies by Mazolla et al. [3], Christianen et al. [12] and Roe et al. [16], evaluation at 6 or 12 months post completion of treatment was more likely to predict subsequent dysphagia. Hence a longer follow up is required in our study to ascertain whether the improvement in swallowing functions persisted. Whether the improvement in swallowing function is due to DARS sparing or because of regression of tumour remains unanswered in our trial. However our trial is noteworthy for some reasons. We were able to achieve sparing of the constrictors and we assessed the impact on swallowing function both subjectively by MDADI and objectively by FEES.

CONCLUSION

DARS optimised radiotherapy with SIB-VMAT is feasible in patients with head and neck cancers. It has the potential to decrease the severity of dysphagia without compromising on oncological outcomes. In our study, DARS sparing resulted in an improvement in the composite MDADI scores at 3 months post-treatment indicating an improvement in swallowing function. The subjective improvement in swallowing function was also confirmed objectively by functional endoscopy(FEES). DARS sparing should become the standard of care in the treatment of head and neck cancers.

Statements

The study was done in accordance with Good Clinical Practice Guidelines and the Declaration of Helsinki and was approved by our institutional ethics committee (JIP/IEC/ 2017/0467) on March 8, 2017.

Written informed consent was obtained from participants to participate in the study.

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