

Prospective subjective evaluation of swallowing function and dietary pattern in head and neck cancers treated with concomitant chemo-radiation

ABSTRACT

Aim: Prospective subjective evaluation of swallowing function and dietary pattern in locally advanced head and neck cancer patients treated with concomitant chemo-radiotherapy (CRT).

Materials and Methods: Prospective evaluation of swallowing function with performance status scale for head and neck cancer patients (PSSHN) at pre-CRT, CRT completion and at subsequent follow-ups in adult with loco-regionally advanced head and neck squamous cell carcinoma (HNSCC) patients.

Results: In 47 patients (40 male, seven females; mean age 53; 72% smoker 53%, oropharyngeal cancer), the mean total PSSHN score at pre-CRT was 258.5 and decreased to 225.2 and 219.2 at two and six months respectively. Understandability of speech, normalcy in diet and eating in public at pre-CRT and six months were 91.5 and 84.4; 80.4 and 63.1; 87.3 and 76.6 respectively. In univariate analysis, pre-CRT PSSHN scores were significantly lesser in patients with severe pre-CRT dysphagia ($P = 0.001$), hypopharyngeal cancer ($P = 0.244$) and advanced T-stage (T3/4) disease ($P = 0.144$). At CRT completion, there was significant reduction of PSSHN scores in patients with severe pre-CRT dysphagia ($P = 0.008$), post-CRT weight loss ($>10\%$) and disease progression ($P = 0.039$). At two months and six months, 17 (57%) and 11 (73.5%) patients respectively showed change in dietary habit. Mean increase in meal time was 13% and 21% at two and six-month follow-up.

Conclusions: HNSCC patients show deterioration in swallowing function after CRT with normalcy of diet in maximum and eating in public least affected. Pre-CRT severity of dysphagia, weight loss $>10\%$ and disease progression have significant correlation with higher swallowing function deterioration after CRT.

KEY WORDS: Chemo-radiotherapy, developing countries, head and neck cancer, pattern in locally advanced head and neck, swallowing function

INTRODUCTION

In today's era, organ preservation is an important mile stone in the management of head and neck cancer. In loco-regionally advanced head and neck cancer concurrent chemo-radiation (CRT) is considered the standard of care for organ preservation.^[1] Several large randomized studies and meta analyses have convincingly proven the equivalent survival with organ preservation approach compared with radical resection.^[1-3] However, though organ preservation is possible with radiation therapy (RT), in recent years, a new debate regarding the 'functional status' of preserved organ with radiation has been started.^[4] A few oncologists have shown serious doubt regarding the functional integrity of the preserved organ and thus utility for organ preservation at least in a subset of patient. Some believe that 'non

functioning organ preservation' may cause more harm to the patient than complete excision.^[5] The present day demand is to have 'functioning organ preservation,' which maintains and /or improves the quality of life.

A few small prospective and retrospective series have documented the functional status in loco-regionally advanced head and neck cancer of the organ after CRT.^[6-8] However, literature is especially lacking in prospective detailed subjective and objective assessment of swallowing function. Thus, the onus is on the treating oncologists to provide functional outcome results of organ preservation with prospective studies involving large number of patients. The toxicity profile of patient not only depends upon the treatment modality used but also on patient related factors (e.g. nutritional status). Patient factors may vary with geographic

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and socio-economic status, thus it is imperative to have the toxicity profile in different patient population.^[8,9] On the other hand, pre-RT functional data is also important to provide impact of CRT at both early and long term functional outcome. The complex nature of assessment and interpretation of swallowing function may be the major reason for the limited prospective data. Impairment of swallowing function may be due to dryness of mouth (xerostomia), pain during deglutition, mucositis or even radiation induced fibrosis of 'dysphagia aspiration related structures' (DARS).^[10,11] Prospective objective evaluation may determine the impact of radiation on long term swallowing dysfunction. Consequences of dysphagia include dehydration, starvation, weight loss, aspiration pneumonia, airway obstruction and may also a cause of early mortality.^[12-13] Dysphagia may be in the form of 'labored' swallowing, prolonged eating times and limited range of foods that can be swallowed.

In the present analysis, early prospective swallowing function evaluation is done with both subjective and objective methodology at pre and post-radiation and compared with different patient related parameters.

MATERIALS AND METHODS

In the period from September 2007 to November 2008, 47 consecutive head and neck cancer patients who were planned for RT and had fulfilled the present study criteria were accrued prospectively after procuring informed consent from the patient. This study was approved by the institutional scientific and ethics committee, which prospectively accrued histologically confirmed loco-regionally advanced (T1-4 N0-3 M0) non-nasopharyngeal squamous cell carcinoma patients (>18 years) of head and neck region (oropharynx/ hypopharynx / larynx) with good performance (KPS \geq 70) and nutritional status. Patients with prior history of surgery, therapeutic irradiation (head and neck region) or chemotherapy were excluded. Majority of the patients were treated with conventional bilateral portal with reducing field technique (66-70 Gy / 33-35 #). In conformal radiotherapy (3 DCRT/IMRT), standard dose (GTV: 70 Gy / 30#, CTV: 60 Gy / 30#, 54 Gy / 30#) and constraints were prescribed. All Stage III/IV patients and four patients of Stage II with bulky disease received concomitant chemotherapy (cisplatin 30 mg / m² weekly). All patients were reviewed weekly for assessment of compliance to treatment, weight loss, performance status (KPS), skin and mucosal reactions (RTOG toxicity criteria), blood counts and need for supportive care (e.g. Ryle's tube, nutrition supplement). During treatment, patients were prescribed analgesics and local anesthetics. Pre-CRT swallowing function evaluation was done with subjective scale (Performance Status Scale for Head and Neck Cancer Patients [PSSHN]) and subjective dysphagia function was evaluated using standardized scale.^[14,15] In subjective dysphagia, evaluation score ranges from 0 to 6. Score 0 suggests no dysphagia and score 6 suggests 'nothing by mouth'. PSSHN is a questionnaire method for

evaluation of subjective swallowing function. It has eating in public, understandability of speech and normalcy of diet domains. Each domain maximum and minimum scores were 0 and 100 respectively. Maximum total score is 300. Higher score indicates better swallowing function.

All the data was collected prospectively and analyzed with SPSS version 15. Demographic characteristics and results were summarized using mean, percentages, medians, and ranges. Pre-CRT, early post-treatment (two months post-CRT) and late post-treatment (six months post-CRT) parameters (KPS, weight loss, PSSHN) and side effect ratings were analyzed and compared using paired and unpaired t-test as appropriate.

RESULTS

Among the 47 patients analyzed, there were 40 male, seven females; mean age 53 years (range 40-65 years); 72% smokers and with preserved performance (KPS >70) and nutritional status [Table 1]. Locally advanced oropharyngeal cancers (53%) were most common with commonest sub-site being base of tongue and pyriform fossa in oropharynx and hypo pharynx respectively. All patients completed CRT without any significant modification in treatment schedule.

At the time of analysis, all (n = 47) patients had completed two months and 26 patients had completed six-month follow-up. Among them, at two-month evaluation, one patient had died and 46 had follow-up evaluation. At six months, 19 patients

Table 1: Patient demographic profile (n=47)

Age (years)	Median (range)	51 (40-65)
Gender	Male	40 (85%)
	Female	7 (15%)
Personal habits	Tobacco chewer	33 (70%)
	Smoker	34 (72%)
	Alcohol User	17 (36%)
Presenting symptoms	Difficulty in swallowing	36 (76%)
	Pain while swallowing	3 (10%)
	Foreign body sensation in throat	2 (7%)
	Swelling in neck	2 (7%)
Baseline severe dysphagia (Gr.3-6)*	Yes	19 (40%)
	No	28 (60%)
Primary site	Oropharynx	25 (53%)
	Hypopharynx	16 (34%)
	Larynx (Supraglottic)	6 (13%)
T-stage	T1-2	19 (40%)
	T3-4	28 (60%)
Nodal stage	N0-1	29 (61.7%)
	N2-3	18 (38.3%)
AJCC Stage	I-II	11 (24%)
	III	19 (40%)
	IVA	17 (36%)
Primary tumour volume (cm ²)	Mean (SD)	16 (\pm 5.8)
RT Techniques	Conventional	39 (83%)
	3D CRT / IMRT	8 (17%)
Concurrent chemo-radiotherapy	Yes	40 (85%)
	No	7 (15%)

*Grade of dysphagia according to the standard symptom scale (Waxman et al; 1990)

had PSSHN evaluation, six died with disease progression and one patient was lost to follow-up.

Detailed PSSHN scores at pre-CRT and at subsequent follow-up were mentioned in Table 2. Mean total score for PSSHN scale at pre-CRT was 258.5 and decreased to 225.2 at 2 month and 219.2 at 6 month follow up respectively. Normalcy of diet was 80.4 at pre-CRT and was reduced to 63.1 at two-month post-CRT. Eating in public domain score was 87.3 at pre-CRT, 76.1 at two months and was maintained to 76.6 at six-month follow-up. There was minimal disturbance in patient's speech with more than 77% patients' speech always understandable and 23% patients requiring occasional repetition of words. Half of the patients (50%) reported being comfortable eating in public places. 'Understandability of speech' was minimally affected whereas 'normalcy in diet' was impaired most at post-CRT evaluation [Figure 1].

At pre-CRT evaluation, on univariate analysis, PSSHN score was significantly poor in patients with severe pre-CRT dysphagia score (dysphagia Grade 3-6) ($P = 0.001$) compared with patients with preserved dysphagia function (Grade 0-2) and markedly less in patients with hypo pharyngeal than non-hypo-pharyngeal cancer ($P = 0.244$) [Table 3]. Lower T-stage (T1-2) patient's had better pre-CRT PSSHN score (276.3 versus 254.1; $P = 0.144$), However, patient related factors (age, gender), personal habits (smoking, tobacco chewing, alcohol

use) or treatment related factors (overall treatment time) had not shown to significantly influence pre-CRT PSSHN score.

Patients with severe pre-CRT dysphagia (Grade 3-6) ($P = 0.008$), significant weight loss ($>10\%$) at CRT completion and patients with disease progression ($P = 0.039$) had significantly higher reduction of PSSHN score at follow-up [Table 4]. Patient-related factors such as age ($P = 0.793$), gender ($P = 0.426$), personal habits ($P = 0.799$), pre-RT hemoglobin levels ($P = 0.218$), site of primary ($P = 0.536$), T stage ($P = 0.406$), nodal stage ($P = 0.782$), AJCC stage, ($P=0.412$), overall treatment time ($P = 0.190$), grade of mucositis at RT completion ($P = 0.538$) and weight loss $>10\%$ at two months ($P = 0.186$) evaluation had not shown any significant correlation with reduction in PSSHN score. Smokers, patients with early stage disease (T and N), smaller tumor volume (15 cm^2), overall treatment time > 48 days and with severe mucositis at RT completion had comparatively higher reduction in PSSHN score after CRT, though statistical significance was not achieved.

At pre-CRT, 31 patients (65%) were on solid diet, 16 (33%) on semisolid and only one patient (2%) was on liquid diet. At two-month and six-month post-CRT follow-up 33% and 26% patient were on solid food [Figure 2]. At CRT conclusion, 11 (23.5%) patients were on feeding tube and at two months post-CRT; there were 12 (27%) .

Among the 31 patients on solid food at pre-CRT, 30 patients had two-month and 15 had six-month follow-up [Table 5].

Table 2: PSSHN score at pre-CRT and in different follow up [Mean (±SD)]

PSSHN Parameter	Pre-CRT (n=47)	2 month (n= 45)	6 month (n= 19)
Eating in public	87.3 (±13.7)	76.1 (±15.9)	76.3 (±17.6)
Understandability of speech	91.5 (±12)	84.4 (±17.9)	81.6 (±20.1)
Normalcy of diet	80.4 (± 19.9)	63.1 (±22.5)	62.6 (±21.6)
Total Score	258.5 (±38.4)	225.2 (±48.3)	219.2 (±50.8)

PSSHN= Performance Status Scale for Head and Neck Cancer Patients; CRT= Chemo-radiotherapy

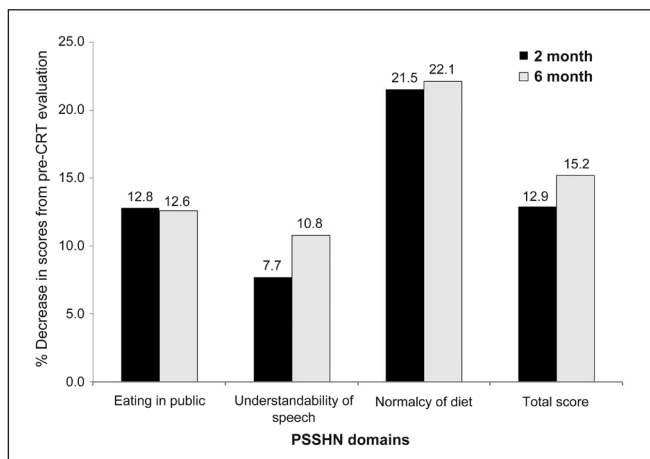


Figure 1: Percentage (%) decrease in PSSHN domain Scores at two and six-month follow-up from pre-CRT evaluation scores

Table 3: Univariate analysis of patient related factors on pre-CRT PSSHN scores

Factors	Parameters	Mean PSSHN score	P-value*
Age	<50 yrs	269.1	0.488
	≥50 yrs	258.4	
Gender	Male	264.6	0.432
	Female	247.5	
Smoking habit	Smoker	261.1	0.790
	Nonsmoker	265.6	
Tobacco	Tobacco Chewer	256.1	0.160
	Non-chewer	279.4	
Site	Non hypopharyngeal	267.4	0.244
	Hypopharyngeal	249.0	
Tumor volume	<15 cc	263.8	0.773
	>15 cc	259.2	
T stage	T1-2	276.3	0.144
	T3-4	254.1	
N stage	N0-1	269.1	0.256
	N2-3	252.0	
AJCC stage	I/II	279.0	0.313
	III/IV	259.0	
Pre-CRT dysphagia	Gr. 0-2	278.2	0.001
	Gr. 3-6	230.5	
Pre-CRT Hemoglobin	≤12 gm	260.7	0.905
	>12 gm	262.8	
Mucositis at CRT conclusion	Gr.0-1	293.5	0.015
	Gr. >2	252.8	

*PSSHN= Performance Status Scale for Head and Neck Cancer Patients

Table 4: Factors influencing decrease in total LIST scores at subsequent follow up from pre-CRT baseline scores

Factors	Parameters	2 month post-CRT			6 month post-CRT		
		% Pts	Mean ↓ in PSSHN Score from pre-CRT	P value	% Pts	Mean ↓ in PSSHN Score from pre-CRT	P value
Age	<50 yrs	37	30.0	0.897	44	47.8	0.793
	≥50 yrs	63	32.1		56	53.9	
Smoking	Smoker	73	36.4	0.268	33	55.0	0.799
	Non-smoker	27	17.5		77	49.1	
Tobacco	Tobacco-Chewer	73	26.0	0.231	75	49.1	0.752
	Non-chewer	27	46.2		25	57.5	
Site	Oropharynx	66	29.7	0.636	60	56.1	0.536
	Hypopharynx	34	37.5		40	40.8	
Tumour volume	≤15 cc	50	46.5	0.179	62	54.4	0.954
	>15 cc	50	24.6		38	56	
T stage	T1-2	37	45.5	0.151	50	60.6	0.406
	T3-4	63	23.2		50	41.8	
N stage	N0-1	63	34.4	0.587	75	52.9	0.801
	N2-3	37	25.9		25	46.3	
AJCC stage	I/II	20	38.3	0.645	31.3	65.0	0.412
	III/IV	80	29.6		68.7	45.0	
Overall T/t time	≤48 days	76	16.8	0.246	37.5	32.5	0.190
	>48 days	24	36.6		62.5	62.5	
Mucositis at CRT completion	Gr.0-1	23	22.8	0.538	43.8	55.7	0.730
	Gr. >2	77	33.9		66.2	47.7	
Pre-CRT dysphagia	Gr. 0-2	66	18	0.008	82	51.2	0.986
	Gr. 3-6	34	58		18	51.6	
Pre-CRT Hb	≤12 gm	23	25.0	0.646	25	27.5	0.218
	>12 gm	77	33.2		75	59.1	
Disease status at last follow up	Alive with no disease	80	28.3	0.928	81	40.7	0.039
	Progression / dead	20	43.3		19	96.7	
% wt loss at 6 months	≤10%	60	12.7	0.309	60	38.3	0.186
	>10%	40	32.8		40	67.9	

PSSHN = Performance Status Scale for Head and Neck Cancer Patients; CRT= chemo-radiotherapy; Hb= hemoglobin; ↓ suggests deterioration in PSSHN scores from pre-CRT scores

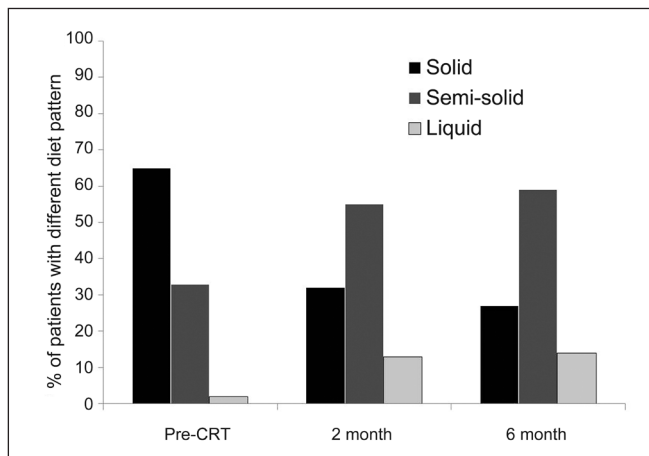


Figure 2: Diet pattern at pre-CRT and subsequent follow-ups

Among these patients, at two-month and six-month evaluation, 17/30 (57%) and 11/15 (73.5%) patients respectively required change in dietary habit to semisolid or liquid food. Mean increase in meal time in patients on solid food were only 13% and 21% at two and six-month follow-up from pre-CRT assessment. Weight loss was 8.8% at post-CRT two months and only 2.9% at six-month follow-up.

Table 5: Change in diet pattern in patients* (n=31) on solid diet at pre-CRT to semisolid/liquid diet at subsequent follow ups

Parameters	Pre-CRT (n = 31)	2 month (n = 30)	6 month (n = 15)
Food consistency-Solid	31(100%)	13(43%)	4(26.5%)
Food consistency-Semisolid	-	16(53.5%)	8(53.5%)
Food consistency-Liquid	-	1(3.5%)	3(20%)
Mean meal time of pt on solid diet (min)	21.5 ±5.2	24.3 ±8.4	26 ±5.5
Increase in meal time in patients on solid diet [min (%)]	-	2.8 (13%)	4.5 (21%)
Diet conversion rate at follow up	-	56.7%	73%
Weight (Kg)			
Mean (SD)	53.2±12.8	48.5±13.0	47.1±11.4
% Weight loss from previous follow up	-	8.8%	2.9%

*Patients on solid diet before CRT was only considered in present analysis

DISCUSSION

In recent years, there has been great enthusiasm regarding quality of life, acute and late toxicities of different treatment modalities and these are being recognized as equally important as survival function.^[10-12,16] Prospective measurement of toxicity outcome is a tedious process but is critical in providing

substantial evidences regarding the magnitude of toxicity with any treatment modality. Toxicity outcome not only depends on the treatment modality but is also closely related with various patient factors. Literature suggests that higher proportion of patients in developing countries have advanced disease at presentation compared with the developed country data.^[17] Hence, toxicity profile of patients from developing countries with larger volume disease and poorer nutritional status may be different from developed countries. Implementation of 'treatment guidelines' obtained from western population should be appropriately adapted only after evaluation of toxicity parameters in the patient population concerned.^[8]

In head and neck cancer, CRT is known to cause deterioration of swallowing function in both early and late post-CRT period.^[18-20] CRT is the accepted standard of care as organ preservation strategies in loco-regionally advanced HNSCC, however, it is imperative for clinicians to assess the increased risk of dysphagia and aspiration with this treatment.^[12-13] Disease itself, poor oral hygiene, throat pain, mucositis, xerostomia, impairment of 'dysphagia aspiration related structures' (DARS) and also psychosocial factors plays adverse role in swallowing.^[10,11,1,18,21] Though dysphagia has been described as an important acute and late toxicity of RT with or without CT, there is very sparse data regarding its objective assessment, especially from developing countries.

In our study, most of the patients had deterioration of total and sub-domain PSSHN scores at post-CRT follow-up evaluation. These findings matched with that of Stenson *et al.* and Salama *et al.* study which reported 60% patients had a worse dysphagia severity score after CRT.^[22,23] Normalcy of diet is mainly affected at two months post-CRT and was shown to deteriorate further in subsequent follow-ups. Magnitude of deterioration of total PSSHN scores at post-CRT evaluation corroborated consistently with the published western literature.^[14,17-19,24] However, eating in public and understandability of speech is minimally affected in our patients. This may be due to influence of socio-cultural environment rather than treatment modality used. Patients had higher dysphagia scores due to acute toxicities of CRT at immediate post-CRT period, which decreased at two and six- month follow-up evaluation as reflected in PSSHN scores.

In literature, HNSCC patients treated with CRT had significantly higher swallowing dysfunction compared with RT alone.^[14,18] In RTOG 91-11 study, only 23% of patients treated with

CRT (Cisplatin) were able to swallow soft foods at post CRT evaluation compared with 15% in RT alone arm and Only 9% patients on sequential Cisplatin/Fluorouracil had severe dysphagia.^[24] The mean PSSHN scores of different prospective studies using conventional radiation therapy are described in Table 6. The mean scores of different domains were similar in our study compared with the published western literature.

Patient and tumor related factors had influenced the change in PSSHN scores at post-CRT evaluation. Hypopharyngeal tumors, smokers, larger primary tumor volume, longer treatment time (> 48 days), patients with post-CRT >10% weight loss, severe baseline dysphagia and disease progression are prone to have higher post-RT swallowing function deterioration. This suggests preservation of structure by itself does not ensure preservation of function. However, age at presentation, AJCC stage and pre-CRT hemoglobin level did not significantly influence post-CRT PSSHN scores. As expected, though T-stage had significant impact on swallowing function, N stage did not show any correlation. Longer treatment time may be due to treatment interruptions caused by severe acute toxicities during treatment, suggesting patients with high acute toxicities are also prone to have late squeals of CRT.^[25] In literature, large primary tumor, hypo pharyngeal tumors and patients with disease progression had poorer post-treatment swallowing function.^[7,9,20]

Mean weight had persistently reduced at subsequent post-CRT follow ups. Average weight loss was 8.5 kilograms from pre-CRT assessment and was matched with Connor *et al.* study.^[24] Maximum reductions in weight was observed in immediate post-CRT two-month period, minimum during two to six months and there was a trend of increase in weight loss after six-month follow-up. In immediate post-CRT period, severe acute mucosal toxicity, change in taste, CRT-induced dysphagia and also anorexia played a role in weight reduction. In addition, xerostomia and inadequate dietary intake also contributed to weight loss. Majority of our patients had changed their dietary habits at subsequent follow-up. Conversion rate from solid to semisolid/ liquid food was high at follow-up. Our findings corroborated with Graner *et al.* and Machtay *et al.* findings who reported poor mean normalcy of diet score after CRT in head and neck cancer.^[18,19] List *et al.* also reported persistent restricted dietary habitat post CRT one year follow up evaluation.^[17] There was only minimal increase in meal time in patients on solid food at follow-up.

Table 6: Comparison of PSSHN scores obtained from literature

Author	Year of publication	RT methods	n	Eating in public	Understandability of speech	Normalcy of diet
Harrison <i>et al.</i> ^[26]	1996	Conv. CRT	36	84	96	73
List <i>et al.</i> ^[27]	1999	Conv. CRT	64	74	74	51
Allal <i>et al.</i> ^[14]	2000	Conv. CRT	21	89	84	86
Machtay <i>et al.</i> ^[18]	2002	Conv. CRT	53	67	65	97
Graner <i>et al.</i> ^[19]	2003	Conv. CRT	11	42	-	29
Fung <i>et al.</i> ^[3]	2005	Conv. CRT	56	74	63	48
Present study	2010	Conv. CRT	47	76	81	62

Conv. CRT= conventional chemo-radiotherapy; RT= radiotherapy; n= number of patients accrued

Patients were encouraged to have feeding tube as and when required. However, acceptance of feeding tube was low in our patient population and only a small proportion of patients had naso gastric tubes while none had percutaneous endoscopic gastrostomy tube (PEG) insertion. Patients were strongly encouraged to maintain oral intake with high calorie diet as long as possible during treatment. In prospective organ preservation studies from developed countries 88% of patients were either on PEG or Ryle's tube feeding.^[2,3] On the contrary, in our study only 27% had feeding tube at two-month evaluation.

Though our study provides interesting information regarding swallowing function at pre-CRT and post-CRT follow-up, it is not devoid of limitations. In the era of conformal RT, majority of our patients were treated with 2-dimensional simulator based planning. PSSHN scoring methodology has not been validated in patient population from developing countries. In recent years, a lot of emphasis has been given to dysphagia aspiration related structure (DARS) and their constraints. Swallowing function is inherently related to DARS function and it will be interesting to see the outcomes with IMRT when appropriate DARS constraints are used.^[20] However, in our study, the small cohort of patients treated with IMRT had not shown any significant preservation of PSSHN scores at post-CRT follow-up. All patients with abnormal swallowing should be encouraged for swallowing therapy and preferably take semisolid diet orally during and post-CRT period. At follow-up, special attention and appropriate referral should be given towards dietary advice.

In summary, the data clearly establish that CRT causes deterioration of swallowing function in majority of HNSCC patients. Normalcy of diet is mostly affected after RT. Conversion from solid to semisolid / liquid food was observed in majority of the patients. Eating in public was least affected and mainly due to socio-cultural reason. Patients with higher pre-CRT dysphagia score, weight loss >10% and disease progression have significantly higher swallowing dysfunction after CRT. After six-month evaluation, there was a trend of higher weight loss, which may have been due to reduction in intensity of supervision, poorer compliance or due to disease progression. Dietary supervision needs to be reinforced for a longer duration after CRT. Larger and longer studies are needed to validate the data.

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