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Psycho-oncology/Supportive Care in Head–Neck Cancers Patients Undergoing Radiation Therapy: A Randomized Controlled Trial

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Abstract

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Keywords

► distress
► head–neck cancer
► palliative care referral
► psycho-oncology referral
► quality of life
► supportive care

An elevated level of distress is associated with poor health-related quality of life (QoL), decreased patient satisfaction, poor treatment compliance, and possible reduced survival. This randomized trial, conducted at a single center in India, enrolled head–neck cancer patients aged > 18 years who were undergoing curative intent radiation therapy, and had significant baseline distress as per the National Comprehensive Cancer Network distress thermometer (distress score ≥ 4). The patients were randomized into the Standard arm (STD), which involved routine assessment by the oncologist, or the Interventional arm (INV), where psycho-oncology/palliative/supportive care referral was done at baseline and every week during treatment. The study's primary endpoint was the proportion of patients having significant distress 6 months' posttreatment. A total of 212 patients were randomized ($n = 108$ STD, $n = 104$ INV). At 6 months' post-treatment completion, 90 and 89 were evaluable in the STD and INV, respectively. The median distress score was 2 in both arms at this time point. There was no significant difference in the proportion of patients having significant distress in STD versus INV (9 vs. 15.6%, $p = 0.20$). There was an improvement in any symptom measured by the Edmonton Symptom Assessment Score (pain, tiredness, drowsiness, nausea, lack of appetite) and the QoL for the entire cohort with no statistically significant difference between arms for symptoms, QoL, or survival endpoints. Psycho-

oncology and palliative/supportive care referral did not impact distress, symptom burden, QoL, or survival at 6 months' posttreatment completion significantly in this randomized trial.

Clinical Trial Registry of India Registration number: CTRI/2016/01/006549.

Introduction

Distress is defined by the National Comprehensive Cancer Network (NCCN) as "a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment."[1] About 30 to 50% of newly diagnosed and recurrent cancer patients show a significant level of distress.[2,3] While cancer-related distress is often amenable to treatment, it is frequently underdiagnosed and thus undertreated, with less than 10% of patients receiving psychosocial help.[4] An elevated level of distress is associated with poor health-related quality of life (QoL), poor compliance to treatment, decreased patient satisfaction with medical care, and possibly reduced survival. It is now being recognized as the sixth vital sign of cancer care.[3,5–8] The NCCN distress thermometer (DT) is the most widely used tool to screen and quantify distress.[9]

Head and neck cancer (HNC) patients experience elevated levels of distress compared with other patients with significant distress reported in 30 to 56% of patients at diagnosis.[5,10–14] Multiple factors associated with higher distress in HNC include the sociodemographic profile, the disease site, the stage at diagnosis, the treatment received, the inability to perform activities of daily living, and the response to treatment.[11,15] While most of these factors remain unmodifiable, psychosocial counselling has been shown to significantly alleviate distress levels and improve physical, mental, and emotional well-being. A pretreatment and during-treatment visit to a qualified counsellor can potentially reduce posttreatment distress, improve treatment compliance, and improve outcomes.[16]

We conducted this randomized trial to assess the impact of psychosocial counselling in HNC cancer patients undergoing radiation therapy (RT).

Materials and Methods

Design

This was an open labeled phase III randomized controlled trial conducted at a tertiary cancer center in India after Institutional Ethical Board approval. The study was registered with the Clinical Trial Registry of India (CTRI/2016/01/006549). The study was conducted according to the International Conference on Harmonisation-Good Clinical Practice and Declaration of Helsinki.

Inclusion/Exclusion Criteria

Patients with HNC aged more than 18 years, Eastern Cooperative Oncology Group Performance Status ≤ 2 planned for curative intent RT $\pm$ concurrent chemotherapy (either definitive or adjuvant) were screened for the study. Patients with prior history of treatment for any other malignancy treatment, any known psychiatric condition, those planned for adjuvant chemotherapy after RT, and those who would likely be unable to fill the questionnaires were excluded. Only patients with a distress score ≥ 4 (as per the NCCN DT) were accrued and randomized in the trial.

Interventions

The patients were randomized into Standard (STD) and Intervention (INV) arms. As per the existing standard of care, patients were assessed by the treating oncologist regarding physical, emotional, and social issues in both arms. Symptomatic pharmacological interventions as deemed suitable were allowed. Appropriate references to pain clinic physician, psychiatrist, social worker, or palliative care physician were done as per the oncologist's assessment in both arms. In the STD arm, patients proceeded to the routine cancer-directed treatment after this. The radiation oncologist and medical oncologist (for patients receiving concurrent chemotherapy) assessed patients once a week for toxicity, and symptomatic medications were prescribed as deemed suitable.

In the INV arm, patients were referred to the psycho-oncology and palliative/supportive care department for further intervention within a week of baseline assessment by the physician. The baseline assessment at the psycho-oncology/palliative/supportive care department consisted of detailed psychiatric history and mental status examination, understanding of concerns and coping skills, assessing global functioning, noting baseline investigations, and ordering further investigations, if required. A palliative care registration number was provided for reference, and a palliative care contact card was provided. The intervention also included assessment by nursing staff for needs specific to cancer and supportive care. A medical social worker and counsellor also assessed the patient for financial and logistical assistance.

Additionally, pain/physical symptoms were assessed, and an individualized management plan was given to the patient. After the initiation of treatment, once weekly assessments were done by the psycho-oncology/palliative/supportive care team, which comprised evaluating changes in preexistent and newly emergent psychological symptoms. Changes in severity and improvement in preexisting physical

symptoms were also noted. The prescribed investigations were documented, and further new investigations were requested, if required. Any other psychological or pharmacological interventions over and above that prescribed by the treating physician were done, and referral to other ancillary services, if required, was given.

The interventions included analgesics/pain medications prescribed by the pain clinic physician, medicines prescribed for anxiety/depression by the psycho-oncologist, counselling by medical social worker, insertion of feeding tube by the dietician/nutritionist, physiotherapy, and rehabilitative exercises by the occupational therapy/physiotherapy, oral hygiene care by nursing staff, and financial assistance by the social worker.

The cancer-directed treatment comprised of standard RT ± chemotherapy (either definitive or adjuvant) as is practiced at our institute.[17–20]

Randomization

Patients were randomized (Block Permuted) into STD and INV arm in a 1:1 ratio with stratification for treatment (definitive vs. adjuvant), concurrent chemotherapy (yes vs. no), age at baseline assessment (< 65 vs. ≥65 years), and primary site (oral cavity vs. nonoral cavity).

Endpoints

The primary endpoint of the study was the proportion of patients having significant distress (score ≥ 4) 6 months after completion of treatment. Patients who came for 6 months for follow-up either with controlled disease or recurrence were eligible for analysis. The study's secondary endpoints were median distress score in both arms 6 months' posttreatment completion, compliance to treatment, event-free survival, and overall survival. All patients were reassessed at 3 and 6 months after radiotherapy completion using the DT, Edmonton Symptom Assessment Score (ESAS) questionnaire, NCCN problem checklist, EORTC QLQ-C 30, and HN35 questionnaires for the outcome measures. All questionnaires were filled by the patients themselves with the assistance of a trained nurse. Information on the various medical treatments and interventions that the patient had undergone since the baseline screening were collected through patient interviews and electronic medical records.

Statistical Analysis

The trial was powered to detect a 20% difference (estimated 45% in the STD arm and 25% in INV arm, effect size: 0.41) in significant distress between the two arms with 80% power and 5% significance level (two-sided), requiring 106 patients in each arm (after accounting for a 10% attrition rate). The estimate was based on the systematic review and meta-analysis published in 2013 by Faller et al.[21] The chi-square test (two-sided) was used to ascertain the difference between the proportion of patients with significant distress levels between the two arms. The difference in numeric variables between the two arms was established using the Mann–Whitney U test. Survival analysis was done using the Kaplan–Meier method, and a difference in survival between

arms was ascertained using the log-rank test. A p-value of ≤0.05 was deemed statistically significant. Statistical analyses were done using SPSS version 26 and R studio version 4.0.3.

Results

Between February 2016 to May 2017, 600 patients were screened, and 212 patients ($n = 108$ STD, $n = 104$ INV) were accrued (►Fig. 1). The primary reason for screen failure was patients not meeting the inclusion criteria ($n = 210$ had a DT less than 4 at baseline, $n = 28$ were unable to fill the questionnaires, $n = 10$ had a synchronous/metachronous primary). For the primary endpoint evaluation at 6 months after completion of RT, 90 (83.3%) patients were evaluable in the STD arm and 89 (85.5%) patients in the INV arm.

The demographic and disease profile of patients in both arms are given in ►Table 1. The majority of the patients were male (81.13%) and were married (92.9%). Most patients had a prior history of tobacco use (55.1%) and belonged to a low socioeconomic background (66.4%). The oral cavity (58%) was the most common primary site, and adjuvant RT (63.2%) was the most common indication for RT. Overall, 52.8% of patients received concurrent chemotherapy. There was no significant difference between any disease/demographic parameters between the two arms.

The proportion of patients with significant distress at 6 months' posttreatment completion were 9% ($n = 8$) in STD arm versus 15.6% ($n = 14$) in INV arm, $p = 0.20$. At 6 months' posttreatment completion, the median distress score was 2 (interquartile range [IQR]: 2–3) in both arms. There was no significant difference in scores in any of the domains of the NCCN distress checklist score (►Table 2, ►Fig. 2A and B).

There was no significant difference in the two arms for any symptoms (ESAS) at baseline or 6 months (►Fig. 3A and B).

There was no significant difference in the two arms for the global QoL or any domains: physical, emotional, cognitive, social, or role functioning (►Table 3).

Survival Outcomes

At a median follow-up of 39 months (IQR:16–53 months), there was no difference in STD arm versus INV arm for 3-year disease-free survival: 55.4% (95% confidence interval [CI]: 45.2–65.6) versus 57.3% (95% CI: 46.9–67.7), $p = 0.78$ and for 3-year overall survival: 73.4% (95% CI: 64–82.8) versus 72% (95% CI: 62.6–81.4), $p = 0.63$ (►Fig. 4A and B).

Discussion

In this randomized trial, psycho-oncology/palliative/supportive care counselling did not significantly impact the distress levels of the patient posttreatment. For the secondary outcomes, the intervention did not demonstrate any significant benefit over the prevailing standard of care, i.e., assessment/counselling by the treating oncologist symptom-directed pharmacological interventions and referral.

Distress is a complex phenomenon with many factors responsible for cancer-induced distress. In a report by Lewis et al, on HNC patients receiving RT, a low socioeconomic
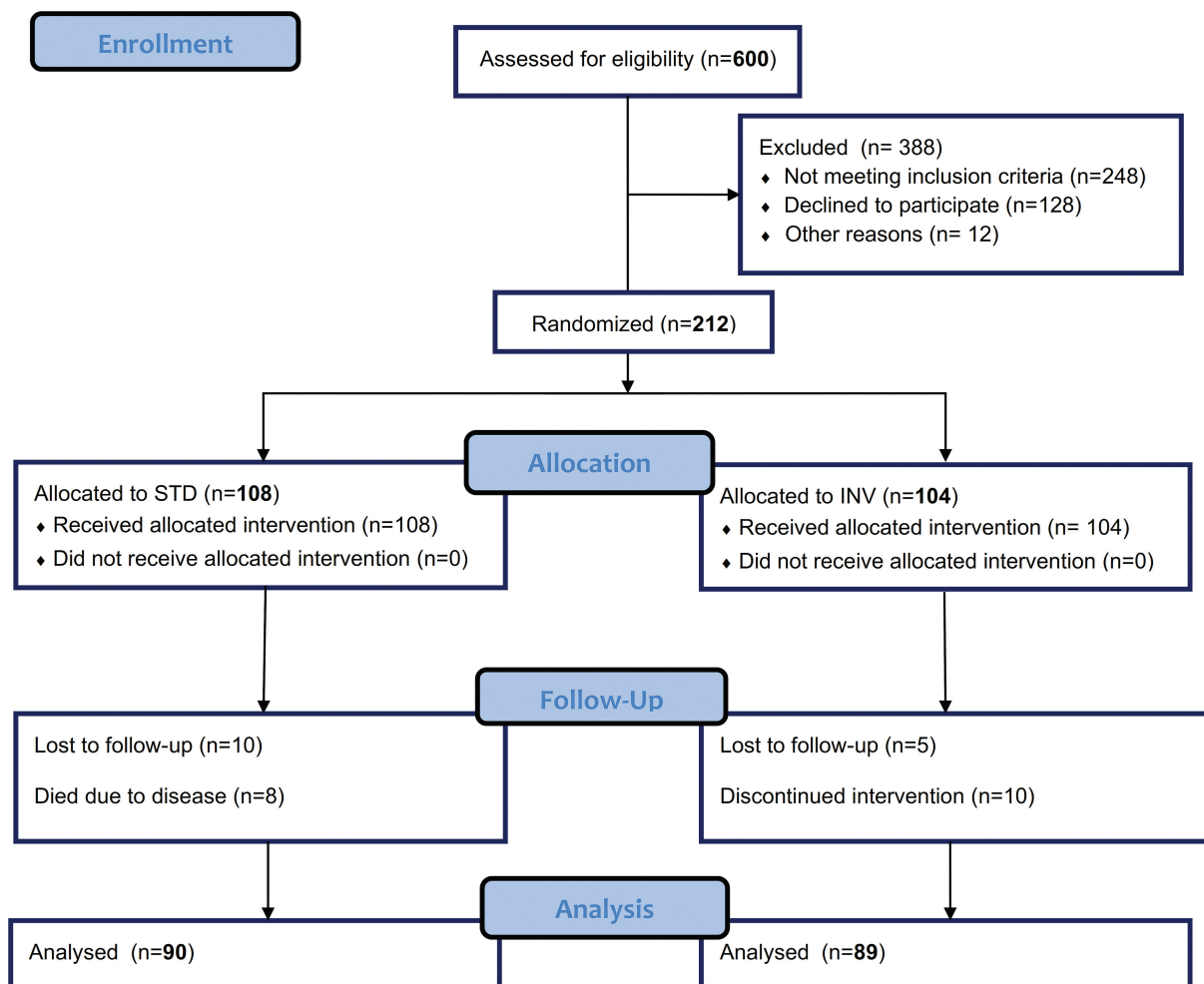
Enrollment

Assessed for eligibility (n=**600**)

Excluded (n= 388)
- Not meeting inclusion criteria (n=248)
- Declined to participate (n=128)
- Other reasons (n= 12)

Randomized (n=**212**)

Allocation

Allocated to STD (n=**108**)
- Received allocated intervention (n=108)
- Did not receive allocated intervention (n=0)

Allocated to INV (n=**104**)
- Received allocated intervention (n= 104)
- Did not receive allocated intervention (n=0)

Follow-Up

Lost to follow-up (n=10)

Died due to disease (n=8)

Lost to follow-up (n=5)

Discontinued intervention (n=10)

Analysis

Analysed (n=**90**)

Analysed (n=**89**)

Fig. 1 Consolidated Standards of Reporting Trials diagram of the study. INV, Intervention arm; STD, Standard arm.

Table 1 Demographic and disease characteristics of study cohort ($n = 212$)

Characteristic	STD ($n = 108$)	INV ($n = 104$)	Total ($n = 212$)	p-Value
Age				0.20
Mean (SD)	51.15 (11.74)	49.05 (12.07)	50.12 (11.924)	
Age group				0.92
< 65 y	93 (86.11%)	90 (86.54%)	183 (86.32%)	
Gender				0.35
Male	85 (78.7%)	87 (83.65%)	172 (81.13%)	
Marital status				0.62
Married	99 (91.67%)	98 (94.23%)	197 (92.92%)	
Education				0.85
Literate	83 (76.85%)	81 (77.88%)	164 (77.36%)	
Occupation				0.88
Employed	84 (77.78%)	80 (76.92%)	164 (77.36%)	
Income				0.73
Low	75 (69.44%)	70 (67.31%)	145 (68.4%)	
Income source				0.89
Self	56 (51.85%)	53 (50.96%)	109 (51.42%)	

Table 1 (*Continued*)

Characteristic	STD (*n* = 108)	INV (*n* = 104)	Total (*n* = 212)	*p*-Value
Addictions				0.61
Any	94 (87.04%)	88 (84.62%)	182 (85.85%)	
Tobacco	57 (52.78%)	60 (57.69%)	117 (55.19%)	
Comorbidities				0.90
Present	18 (16.67%)	18 (17.31%)	36 (16.98%)	
ECOG PS				0.09
0–1	57 (52.78%)	43 (41.35%)	100 (47.17%)	
2	40 (37.04%)	56 (53.85%)	96 (45.28%)	
Disease site				0.92
Oral cavity	63 (58.33%)	60 (57.69%)	123 (58.02%)	
Others	45 (41.57%)	44 (42.31%)	89 (41.98%)	
TNM T stage				0.80
T1	12 (13.9%)	13 (13.5%)	25 (13.8%)	
T2	21 (19.4%)	18 (29.8%)	39 (18.4%)	
T3	23 (21.3%)	21 (20.19%)	44 (20.75%)	
T4a	45 (41.67%)	48 (46.15%)	93 (43.87%)	
T4b	7 (6.5%)	4 (3.85%)	11 (5.19%)	
TNM N stage				0.76
N0	40 (37.04%)	40 (38.46%)	80 (37.74%)	
N1	22 (20.37%)	22 (21.15%)	44 (20.75%)	
N2a	8 (7.41%)	5 (4.81%)	13 (6.13%)	
N2b	23 (21.3%)	19 (18.27%)	42 (19.81%)	
N2c	13 (12.04%)	13 (12.5%)	26 (12.26%)	
N3	2 (1.85%)	5 (4.81%)	7 (3.30%)	
AJCC stage				0.39
I–II	18 (16.67%)	13 (12.5%)	31 (14.62%)	
III	21 (19.44%)	19 (18.27%)	40 (18.87%)	
IV	69 (63.89%)	72 (69.23%)	141 (66.51%)	
Histology				0.52
Squamous cell carcinoma	97 (89.82%)	96 (92.31%)	193 (91.04%)	
RT indication				0.71
Definitive	41 (37.96%)	37 (35.58%)	78 (36.79%)	
Adjuvant	67 (62.04%)	67 (64.42%)	134 (63.21%)	
Chemotherapy				0.74
Yes	58 (53.70%)	54 (51.92%)	112 (52.83%)	

Abbreviations: AJCC, American Joint Committee on Cancer; ECOG PS, Eastern Cooperative Oncology Group Performance Status; INV, Intervention arm; RT, radiation therapy; SD, standard deviation; STD, Standard arm; TNM, tumor, node, metastasis.

status (*p* = 0.04), presence of proliferative growth at presentation (*p* = 0.008), site of the tumor (oral cavity, *p* = 0.02), comorbidity (*p* = 0.04), and presence of Ryle's tube or tracheostomy tube at baseline (*p* = 0.01) were predictors of distress.[11] However, only the patient's socioeconomic status was significant for higher distress levels in the multivariable analysis. Other factors that have been implicated for cancer-induced distress include marital status, gender, education level, tobacco usage, and age. Psychosocial counselling has shown to mitigate some of these risk factors, albeit many of these factors are interrelated, and any intervention for reducing cancer-induced distress will have to address several if not all these factors. While psychosocial/pharmaceutical/surgical interventions can address many factors like pain and cosmetic disfigurement, the sociodemographic causes of distress remain largely unmodifiable. Financial toxicity of

Table 2 Distress scores at baseline and follow-up

	STD ($n = 90$)	INV ($n = 89$)	Total ($n = 179$)	p-Value
Baseline distress score (median [IQR])	6 (5–8)	6 (5–8)	6 (5–8)	0.63
FU distress score (median [IQR])	2 (2–3)	2 (2–3)	2 (2–3)	0.11
Clinically significant distress at FU ($\geq$4)	8 (9.3%)	14 (16%)	22 (12.6%)	0.19
Clinically significant distress at FU ($\geq$5)	2 (2.3%)	6 (6.8%)	8 (4.6%)	0.15
1-point decrease	83 (96.5%)	80 (91%)	163 (93%)	0.12
2-point decrease	72 (83.7%)	68 (77.3%)	140 (88%)	0.28
3-point decrease	53 (61.6%)	48 (54.5%)	101 (58%)	0.34
4-point decrease	30 (35%)	34 (38.6%)	64 (37%)	0.60
Any decrease	84 (97%)	84 (95%)	168 (96%)	0.42

Abbreviations: FU, follow-up (6 months); INV, Intervention arm; IQR, interquartile range; STD, Standard arm.

loss of employment, cancer treatment, and resulting disability has been associated with significant distress in multiple studies.[22,23] While similar conclusive data are lacking from a resource-limited setting, the financial toxicity associated with cancer treatment is likely to be a significant cause of concern in this setting.[24–26]

The reason for no significant improvement in distress scores with psychosocial/supportive care interventions in
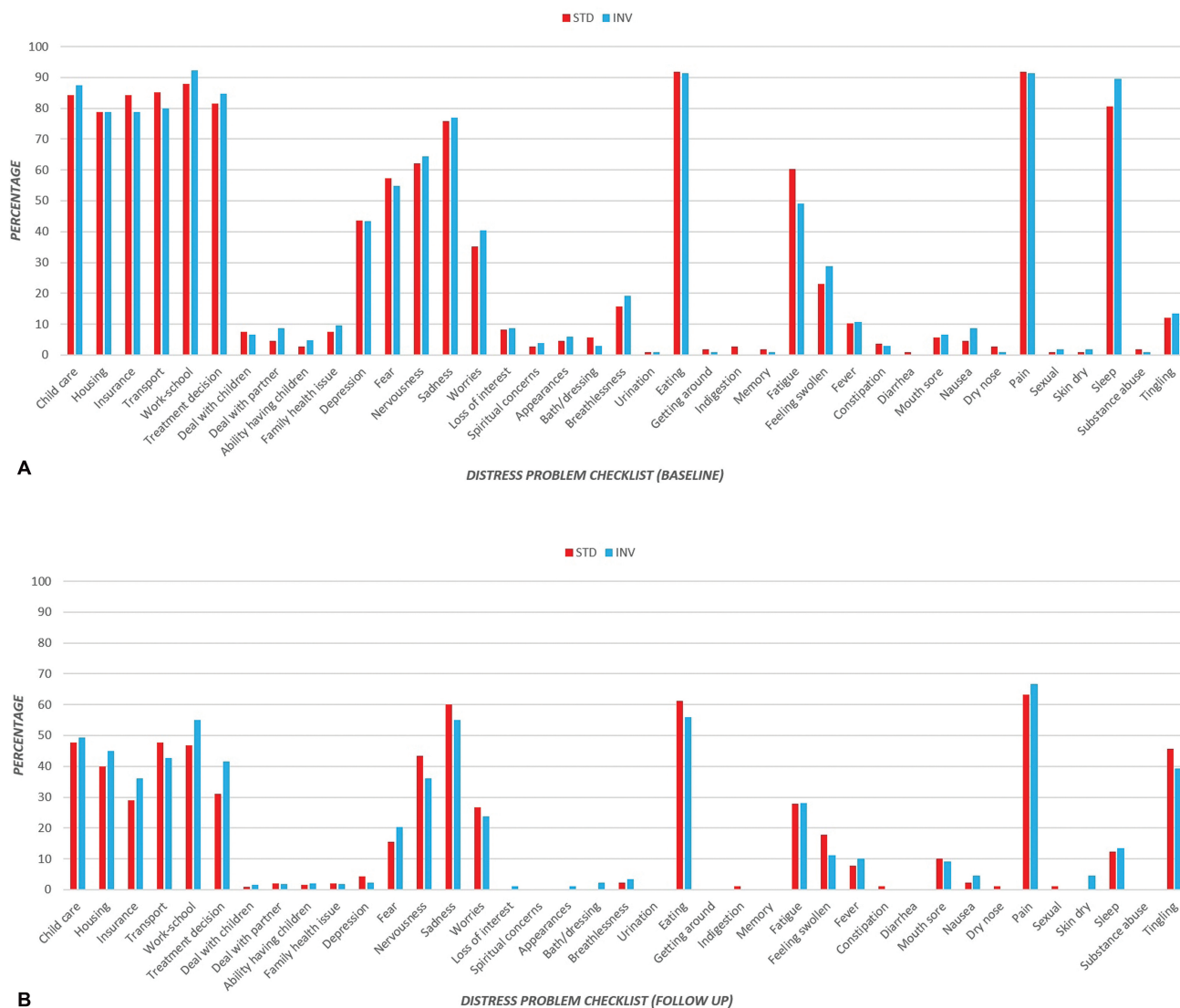

Fig. 2 (A) Distress problem checklist scores at baseline between two arms. (B) Distress problem checklist scores at 6-month follow-up between two arms. INV, Intervention arm; STD, Standard arm.
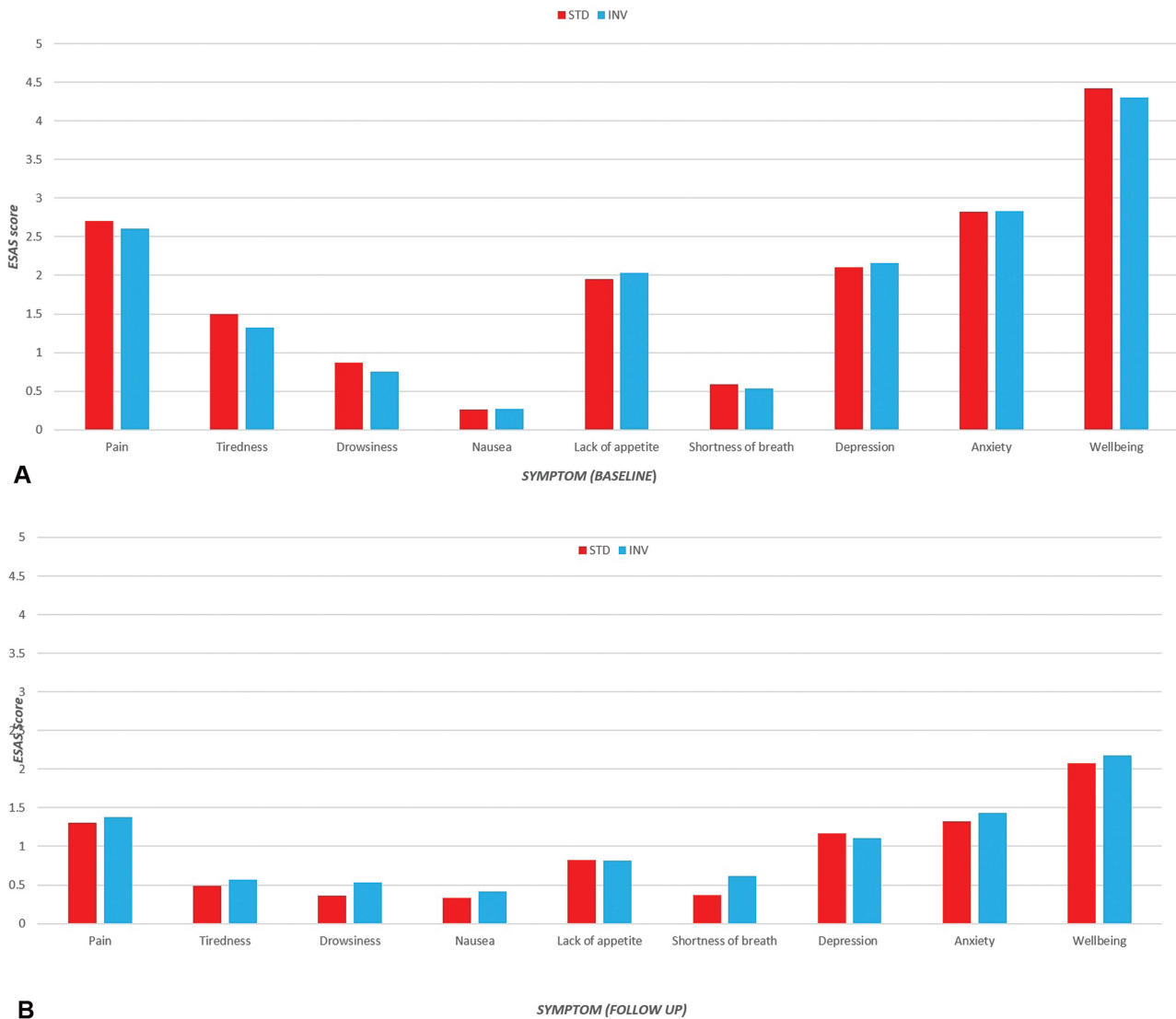
Fig. 3 (**A**) Edmonton Symptom Assessment Score (ESAS) at baseline between two arms. (**B**) ESAS at 6-month follow-up between two arms. INV, Intervention arm; STD, Standard arm.

our trial can be possibly attributed to the prevalence of many nonmodifiable factors leading to distress. Unlike the West, tobacco remains the primary driver of a higher incidence of HNC incidence in India.[27] Head–neck squamous cell carcinomas in India and most other low- or middle-income country are primarily a disease of low socioeconomic status and are associated with a lack of social support, lower education levels, and lack of employment.[28] These significant contributors to distress are unlikely to be mitigated by psycho-oncology counselling, and supportive measures. Recently, a randomized trial to ascertain the impact of (early palliative care [EPC]) referral in advanced HNC was reported from India by Patil et al. The authors reported that more than 40% of patients received financial aid in each arm. Similar to the results of our trial, there was no significant impact on the QoL (FACT HN score $p = 0.94$), ESAS score, and survival.[29] The negative results of these two trials probably point toward the contribution of nonmodifiable background factors, more

than the disease itself, to cancer-associated deterioration in QoL and anxiety.

While patient-reported outcomes (PROs) remain a valuable tool for assessing an intervention's efficacy, there is an element of uncertainty about the generalizability and reliability of PROs. PROs are impacted by other factors such as coping skills, education levels, and priorities.[30,31] Multiple randomized trials have reported discordance between the patient-reported and physician-reported outcomes.[10,29,32]

We used a cut of ≥ 4 for clinically significant distress as per the NCCN 2013 guidelines. However, distress score cut values vary between primary disease sites, race, ethnicity, country, and socioeconomic profile.[9] It is plausible that the cutoff value for significant distress could have been different for the patient population included in this trial, i.e., only HNCs (with a majority being oral cancers) from India.

A similar approach, EPC has improved survival outcomes and QoL in patients with advanced/metastatic tumors of the

Table 3 Median scores of quality of life domains in Standard and Intervention arms at baseline and 6-month follow-up

EORTC QLQ-C30 domains	Baseline			6-month follow-up		
	STD (n = 108) Median (IQR)	INV (n = 104) Median (IQR)	p-Value	STD (n = 90) Median (IQR)	INV (n = 89) Median (IQR)	p-Value
Global QOL	33.3 (16.67–50)	33.3 (16.67–50)	0.62	83.33 (66.67–83.33)	83.33 (66.67–83.33)	0.58
Physical functioning	90 (73.33–100)	86.67 (66.67–93.33)	0.01	100 (100–100)	100 (100–100)	0.76
Emotional functioning	58.33 (41.67–75)	58.33 (50–66.67)	0.69	100 (66.67–100)	91.67 (66.67–100)	0.82
Cognitive functioning	83.33 (83.33–100)	83.33 (66.67–100)	0.61	100 (83.33–100)	100 (83.33–100)	0.57
Social functioning	66.67 (54.17–83.33)	66.67 (50–83.33)	0.54	100 (66.67–100)	100 (66.67–100)	0.23
Role functioning	100 (66.67–100)	100 (66.67–100)	0.48	100 (100–100)	100 (100–100)	0.76
Fatigue	33.33 (22.22–44.44)	33.33 (22.22–44.44)	0.62	0 (0–22.22)	0 (0–22.22)	0.70
Nausea/vomiting	0 (0–0)	0 (0–16.67)	0.49	0 (0–0)	0 (0–0)	0.79
Pain	33.33 (16.67–50)	33.33 (16.67–45.83)	0.77	0 (0–16.67)	16.67 (0–16.67)	0.16
Dyspnea	0 (0–33.33)	0 (0–33.33)	0.74	0 (0–0)	0 (0–0)	0.85
Insomnia	33.33 (0–33.33)	33.33 (0–33.33)	0.38	0 (0–33.33)	0 (0–33.33)	0.87
Appetite loss	33.33 (0–66.67)	33.33 (0–66.67)	0.28	0 (0–33.33)	0 (0–33.33)	0.79
Constipation	0 (0–33.33)	0 (0–0)	0.16	0 (0–0)	0 (0–0)	0.36
Diarrhea	0 (0–0)	0 (0–0)	0.49	0 (0–0)	0 (0–0)	0.15
Financial difficulty	33.33 (33.33–66.67)	33.33 (33.33–66.67)	0.95	0 (0–33.33)	0 (0–33.33)	0.35
Pain	25 (16.6–41.6)	25 (8.3–25.3)	0.24	0 (0–25)	0 (0–25)	0.67
Swallowing	33.3 (0–58.3)	25 (0–50)	0.10	0 (0–25)	0 (0–25)	0.56
Sense problems	25 (0–50)	25 (0–50)	0.45	0 (0–33.3)	0 (0–33.3)	0.88
Speech Problems	33.3 (11.1–44.4)	33.3 (11.1–44.4)	0.67	0 (0–0)	0 (0–0)	0.45
Trouble with social eating	33.33 (33.33–66.67)	33.33 (33.33–66.67)	0.85	33.3 (0–33.3)	33.3 (0–33.3)	0.78
Trouble with social contact	33.3 (0–33.3)	33.3 (0–33.3)	0.66	33.3 (0–33.3)	33.3 (0–33.3)	0.80
Less sexuality	33.3 (0–33.3)	33.3 (0–33.3)	0.67	0 (0–0)	0 (0–0)	0.95
Teeth	0 (0–33.3)	0 (0–33.3)	0.88	0 (0–33.3)	0 (0–33.3)	0.76
Opening mouth	33.3 (33.3–66.6)	33.3 (33.3–33.3)	0.22	0 (0–33.3)	0 (0–33.3)	0.85
Dry mouth	0 (0–33.3)	0 (0–33.3)	0.76	33.3 (0–33.3)	33.3 (0–33.3)	0.67
Sticky saliva	33.3 (0–33.3)	33.3 (0–33.3)	0.56	33.3 (0–33.3)	33.3 (0–33.3)	0.72
Coughing	33.3 (0–33.3)	33.3 (0–33.3)	0.51	0 (0–33.3)	0 (0–33.3)	0.87
Fell ill	33.3 (33.3–66.6)	33.3 (33.3–66.6)	0.88	33.3 (0–33.3)	33.3 (0–33.3)	0.78

Table 3 (Continued)

	Baseline				6-month follow-up			
	STD (n = 108)	INV (n = 104)	p-Value		STD (n = 90)	INV (n = 89)	p-Value	
Pain killers	100 (0–100)	100 (0–100)	0.78		0 (0–100)	0 (0–100)	0.94	
Nutritional supplements	0 (0–100)	0 (0–100)	0.81		0 (0–100)	0 (0–100)	0.89	
Feeding tube	0 (0–100)	0 (0–100)	0.88		0 (0–0)	0 (0–0)	0.85	
Weight loss	100 (0–100)	100 (0–100)	0.56		0 (0–0)	0 (0–0)	0.71	
Weight gain	0 (0–0)	0 (0–0)	0.99		0 (0–0)	0 (0–0)	0.76	

Abbreviations: EORTC QLQ-C30, EORTC Core Quality of Life questionnaire; INV, Intervention arm; QoL, quality of life; STD, Standard arm.

lung, gastrointestinal tract, and head–neck region.[33–35] In head–neck patients treated with curative intent, at least two randomized trials have shown the benefit of psychological/supportive care interventions. In a randomized trial by Krebber et al, patients of head–neck and lung cancer with untreated distress were randomized to standard of care and stepped-up care (comprising of watchful waiting, guided self-help, problem-solving therapy, and psychotherapy and/or psychotropic medication).[12] The recovery rate was better in the stepped care arm at 6 months (55 vs. 29%) and 12 months (46 and 37%). In another randomized trial reported from China in patients undergoing curative-intent RT, patients who received psychosocial interventions ($n = 89$) during RT had an improvement in depression ($p < 0.05$), anxiety ($p < 0.05$), and overall health-related QoL ($p < 0.05$).[36]

In this randomized trial, neither the patient nor the physician was blinded to the treatment allocation. Also, most trials showing a benefit of palliative care/psycho-oncology referrals are in the palliative setting where patients are rarely assessed and treated by all oncology specialties, i.e., surgical, medical, and radiation oncologists. The majority (nearly 60%) of the patients included in this trial included patients who received trimodality therapy. It is plausible that symptoms like pain could have been managed by the oncologists themselves. As per our institutional data, only 5 to 10% patients require dedicated pain care referral for patients receiving Chemoradiation (CTRT). These factors could have contributed to patients receiving adequate psychosocial care by the treating physician(s) themselves in our trial.

One of the strengths of this study lies in the fact that the trial included only patients with significant distress at baseline as has been recommended in multiple previous reports.[21,37] A relatively large number ($n = 212$) of patients were accrued from within a reasonable time. The attrition rate in the trial for the evaluation of the primary endpoint was acceptable in both arms. The cancer treatment protocols were uniform throughout the study. The patients were assisted in filling the questionnaires by trained nursing staff. Another strength of the study was evaluating multiple aspects of psychological well-being, including distress, QoL, and symptom burden.

The primary weakness of the study comes from the fact that there was a gross mismatch between the anticipated distress at 6 months and the actual results. The reasons for the same have been highlighted above. Baseline assumptions in similar future trials should be based on reports from the population where the study is planned rather than extrapolation from a population with a different sociodemographic profile. Another contentious issue can be the time point posttreatment (6 months) for estimating distress as the primary endpoint. This was chosen as some patients with head–neck cancers suffer from acute toxicities for as long as 3 months' posttreatment. A time point of 6 months will possibly limit the impact of acute toxicities on distress levels in the two arms. There is a shortage of dedicated manpower for supportive services like pain management/palliative care in many cancer centers in developing and underdeveloped countries. A referral to dedicated supportive care clinics is
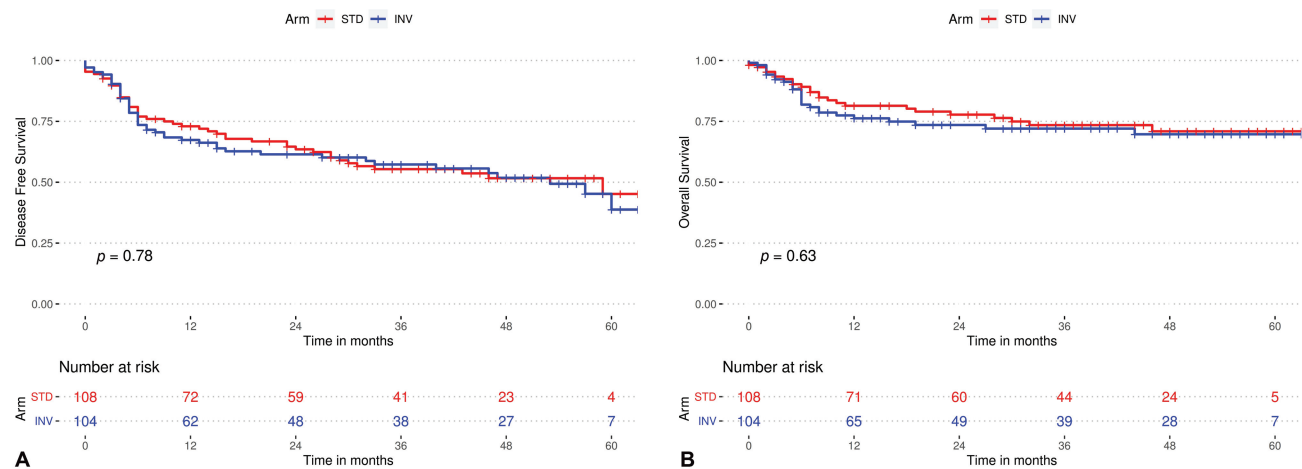
Fig. 4 (**A**) Disease-free survival of the two arms. (**B**) Overall survival of the two arms. INV, Intervention arm; STD, Standard arm.

likely to be a human resource intensive exercise. In our opinion, a sustained benefit for a period of at least 6 months' post-RT could justify a routine incorporation of this approach into clinical practice. However, we accept that the results of the study could have been changed if an endpoint of DS at 3 months or earlier was chosen. Finally, this trial had most patients who received RT post-surgical excision. While we have used surgical excision as a stratification variable, it may be possible that results may be possibly different in a cohort of patients who are treated with definitive RT/CTRT.

Psychosocial and supportive interventions are likely to impact certain cancer patients' psychosocial health positively. However, a dedicated psychosocial referral for all patients in routine clinical practice is resource-intensive in human resources and finances. Hence, future trials should include a larger pool of patients across cancer sites and further focus on identifying suitable patients to make this approach more pragmatic and cost-effective. A reasonable step forward is utilizing a combination of sensitive screening methods that incorporate psychological health parameters, the sociofinancial condition of the patient, the caregiver support, and other logistic issues like transport/lodging.[38,39] Furthermore, while holistic palliative care services cater well to the neediest patient population, i.e., palliative intent patients, perhaps an individualized supportive care approach may be better suited for curative intent patients. Referrals (as per the initial patient assessment) to dedicated pain clinic physicians, psychiatrists, medical social workers, and financial counsellors can be a more resource-sparing and cost-effective approach for such patients.[40] The World Health Organization rehabilitation 2030 goal also emphasizes developing a robust multidisciplinary rehabilitation workforce suitable for country context and promoting rehabilitation concepts across all health workforce education.[41]

Conclusions

To summarize, this trial did not find any significant benefit of early integration of psychosocial/palliative/supportive care on the distress levels, symptom burden, QoL, or survival in

HNC patients undergoing curative-intent RT at 6 months' posttreatment completion. The primary treating physician should continue to assess and intervene for the patients' distress and other psychological needs. Referral to psychosocial/palliative and other supportive care services should be individualized for each patient after screening and ascertaining the main symptom burden of the patient.

Note

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Conflict of Interest
None declared.

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