Original Research Paper

Volume - 12 | Issue - 12 | December - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Oncology/Radiotherapy

SURVIVAL AND LONGTERM TOXICITIES OUTCOMES IN ADAPTIVE INTENSITY-MODULATED RADIOTHERAPY (ART) VS IMRT IN LOCALLY ADVANCED HEAD AND NECK CANCER.

Poonam Chand Bana

ABSTRACT **Background:** Anatomic complexity is a challenge for radiation oncologist.Repeated CT scans and replanning can overcome the variations in terms of size or shape a tumour has undergone during treatment , this process has been termed as Adaptive Radiotherapy(ART). The use of adaptive approach or IMRT-SIB is still under debate since there is not enough evidence of long-term clinical outcomes , metastasis free survival. **Materials And Methods:** Total Sixty patients with locally advanced HNC with a intent to cure were assigned into two arms to receive IMRT up to a dose of 70 Gy with concurrent weekly chemotherapy and were prospectively analyzed between March 2018 and March 2019. Repeat CT scan was acquired after the 3rd week of radiation and those in the study arm were replannned and those in the controlarm continued with the first IMRT plan. For the entire cohort, patients were assessed weekly till the end of treatment and at 1, 3, and6 months, 1 year and 2 years thereafter. Main focus was on Xerostomia status at end of 6 months and end of 2 years and Survival (OS) rates at end of 2-years was calculated and hence compared. **Results:** 2 years overall survival rate was almost similar with 73.33% vs 76.66% in adaptive IMRTand conventional IMRT respectively; p value= 0. 23 Xerostomia was statistically significantly higher in the conventional arm at 6 months(p=0.01).Grade ≥II xerostomia at end of 2 years reduced to 0% vs 4.43 %in adaptive and conventional IMRT respectively (p= 0.78). **Conclusion:** Adaptive IMRT can help to minimise xerostomia at end of 6 months .However no major benefit in survival when compared 2 year after completion of treatment.

KEYWORDS : Adaptive IMRT, head and neck cancer, xerostomia.

INTRODUCTION

Head-and-neck cancer (HNC) ranks sixth most common malignancy worldwide[1], with an annual incidence of more than 80,00,000 cases and 4,31,000 mortality per year[2]. It is ranked third in India registering more than 2,30,000 new cases every year[3]. The male-to-female ratio ranges from 2-4:1 [4]. About 90% of all HNCs are squamous cell carcinomas, higher use of alcohol, tobacco, and betel nut chewing is a major etiological factor[5]. Sixth decade is the median age of diagnosis . Around 60%–80% in developing countries and 40% patients in developed countries are diagnosed in advanced stage . Due to the anatomical complexity of this region where the target volumes are situated near the critical organs such as salivary glands and spinal cord , the treatment becomes a challenging task. The spinal cord lies within a concavity surrounded by the horseshoe-shaped planning target volume (PTV)[6]. Achieving homogeneous dose distribution to PTVs with the conventional radio-therapy (RT) is a difficult task . In these cases Intensity-modulated radiotherapy (IMRT) allows simultaneous pixel-by-pixel intensity modulation of radiation beams and delivery of nonuniform fluence from any given position of the treatment beam to optimize the dose distribution.[7-8]

Using highly conformal techniques has, however, led to the formation of sharp dose gradients, implying that there should be near minimal changes in the patient, tumour, and organs at risk (OARs) position.[10] But such changes may occur owing to the shrinkage of primary tumour and nodal disease from the treatment, alterations in the normal tissue bulk, and position and weight loss.[11-16] This means if we apply the original plan to the altered patient anatomy it may lead to higher-than-intended dose to the surrounding normal structures. To compensate this adaptive radiotherapy (ART) can be used which utilizes repeat computed tomography (CT) scans during the treatment course for replanning according to the alter regional anatomy.[17] In this study we compare the overall survival at 2 years along with xerostomia status at 2 years of ART IMRT vs SIB-IMRT.

MATERIALAND METHOD

A total of sixty biopsy-proven patients of previously untreated locally advanced HNCs were randomized into two arms. All patients were treated with IMRT and given concurrent cisplatin weekly (40 mg/m2) between March 2018 and Nov 2019 at a regional cancer centre in North-Western India and were analyzed as per the institutional review board-approved protocol. Included patients in the study were aged 18–70 years and had Stage III/IV squamous cell carcinoma of head and neck located between the base of the skull up to the thoracic inlet (excluding salivary gland and thyroid tumors). The European Co-operative Oncology Group performance status was 0–2, and baseline organ function test for every patient was adequate (complete blood count, renal function test, liver function test, and others). Exclusion included patients with distant metastasis, recurrent lesions, second malignancies evidence, and severe comorbid diseases .

CT simulation with 3 mm slices was done pretreatment after immbolization . The data were transferred to Eclipse Treatment Planning System v. 13.8 (maker: Varian Medical Systems, Palo Alto, USA) Target volume and normal structures were delineated as per the department protocols. Dynamic IMRT was delivered using 6 MV linear accelerator. Patients were treated with a curative dose of 7000 cGy divided in 33–35 fractions with SIB IMRT and given weekly concurrent chemotherapy , cisplatin (40mg/m^2) .Total dose for PTV 70 was 69.96 Gy in 2.12 Gy daily fraction , PTV 60 received 59.4 Gy with daily dose of 1.8 Gy/#, and PTV 54 received 54 Gy in 1.63 Gy/#.After 3rd week repeat CT scan was acquired for every patient (between16 and 20#s) of radiation, and re-contouring was done. Two plans were generated on repeat scan for each patient; an actual plan (study arm), which was generated by planning again on repeat CT scan, and another hybrid plan (control arm), in which the plan of first IMRT was applied after carefully matching isocenter and bony landmarks. Patients were assessed weekly till the end of treatment and at 1, 3,6 months, 1 year and 2 years. This study aimed to compare overall survival at 2 years and long term xerostomia status between the two arms at end of 6 months and 2 years.

RESULTS

All patients completed the planned treatment with concurrent weekly cisplatin, however seven (23.3%) patients in the conventional arm and three (10%) patients in the adaptive IMRT arm missed 2–3 doses of weekly cisplatin after the 2nd week mainly due to acute toxicities. At about 6 months after treatment completion, 27 (90%) patients in the control arm whereas 29 (96.7%) patients in the study arm achieved CR Upon treatment completion, all patients suffered from RTOG Grade I or II xerostomia in both the arms. As per the CTCAE criteria, there were rates of Grade ≥II Xerostomia in the control (96.7%)and adaptive arms (93.7%) at 6 months post treatment. However,a statistically significantly higher number of patients suffered from Grade III xerostomia at 6 months in the control (50%)compared to the adaptive (30%) arm. (p =0.01)

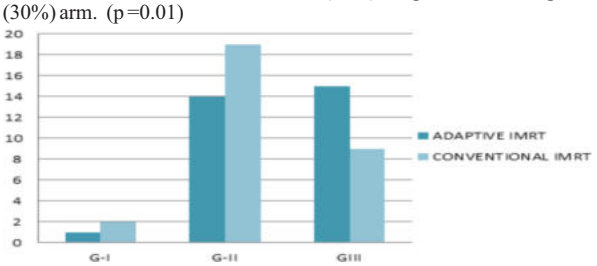


Figure 1: Comparison Of Xerostomia (percentage) At End Of 6 Months In Both Arms .

At the end of 2 years from treatment, there was significant improvement in quality of life and xerostomia where none of surviving patient from both arms complaint of Grade III / IV toxicity, only 4 of 22 (18.18%) and 5 / 23 (21.08%) complaint of erythema, but still can take solid food, corresponds to Grade I toxicity and none vs 1/ 23 (4.34%) in adaptive vs conventional IMRT respectively complaint of difficult at oral intake (Grade II toxicity) .

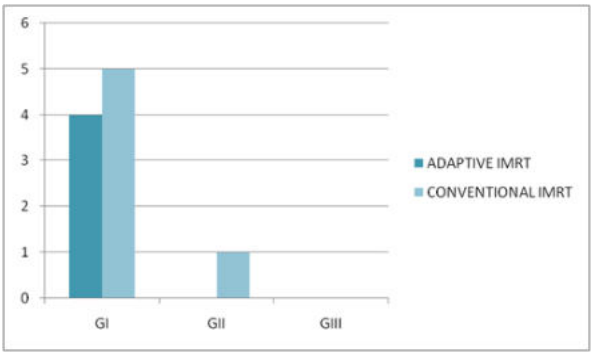
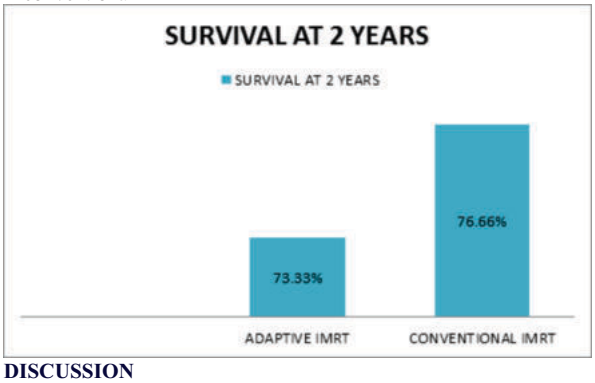


Figure 2: Comparison Of Xerostomia (percentage) At End Of 2 Years In Both Arms.

Overall survival vary a little with 22/30 (73.33%) alive at end on 2 years in adaptive IMRT arm and 23/30 (76.66%) alive at end of 2 years in conventional IMRT



DISCUSSION

The IMRT technique gives the ability to plam treatment fields with varying beam intensity by using inverse planning and iterative optimization algorithms.[18] In the current practice for HNC RT, most centres carry out the first pretreatment plan to completion without accounting for anatomical changes that can occur due to weight loss, tumor shrinkage ,edema, inflammation, and normal tissue volume alterations.[11,19] These volumetric changes could potentially miss marninal geography of tumour or lead to overdosing of the normal tissues during a course of treatment basedon a single-planning data set. ART is a possible solution to account for these errors, which involves repeat imaging and replanning during a course of radiation treatment . The purpose of this study was to verify the potential impact of ART on overall survival, xerostomia for head and neck malignancy.

Our results showed coherence with the prospective study on 22 patients undergoing adaptive IMRT for HNC conducted by Schwartz et al.,[17] which demonstrated equivalent acute toxicity profiles between conventional and adaptive IMRT at 1 year.

Xerostomia rates according to the RTOG criteria were similar in both the arms at the end of treatment and 6 months post radiotherapy. However, rates of xerostomia were statistically significantly lower in the adaptive arm at the end of 6 months, according to the CTCAEguidelines (P = 0.01). Nishi et al[20], in their study of volume and dosimetric changes and initial clinical experience of a two-step adaptive IMRT scheme for twenty patients of HNC, evaluated xerostomia scores 1–2 years after treatment and found that none of the patients complained of Grade 2 or more xerostomia.

The limitation of our study was a small sample size.Further studies with larger sample sizeand longer follow-up are required to validate these results.Furthermore, implemention of ART for routine use is a time- and resource-intensive process. Hence, a more judicious use of ARTwould be to identify patients pretreatment who are more likely to experience significant tumour regression during RT course.

REFERENCES:

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global Cancer Statistics, 2002. CA Cancer J Clin 2005;55:74-108.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
3. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127:2893-917.
4. Kekatpure V, Kuriakose MA. Oral Cancer in India: Learning From Different Populations. National Newsletter and Website from New York Presbyterian Hospital; 2010. Available from: http://www. nypcancerprevention.com/issue/14/cancer _prevention/feature/india. shtml. [Last accessed on 2019 Oct 10].
5. National Cancer Registry Programme. Consolidated Report of the Population Based Cancer Registries. 1990-1996. New Delhi: Indian Council of Medical Research; 2001. Available from: http://www. ncrpindia.org/Annual_Reports.aspx. [Last accessed on 2019 Oct 10].
6. Schelfout J, Derycke S, Fortan L, Van Duyse B, Colle C, De Wagter C, et al. Planning and Delivering High Doses to Targets Surrounding the Spinal Cord at the Lower Neck and Upper Mediastinal Levels: Static Beam-Segmentation Technique Executed by a Multileaf Collimator. Proceedings of the 11th Scientific Symposium of the Belgian Hospital Physicist Association, Gent; 1995. p. 5. Available from: http://hdl. handle.net/1854/LU-253345. [Last accessed on 2019 Oct 10].
7. Dirix P, Nuyts S, Van den Bogaert W. Radiation-induced xerostomia in patients with head and neck cancer: A literature review. Cancer 2006;107:2525-34.
8. Lee N, Xia P, Fischbein NJ, Akazawa P, Akazawa C, Quivey JM. Intensity-modulated radiation therapy for head-and-neck cancer: The UCSF experience focusing on target volume delineation. Int J Radiat Oncol Biol Phys 2003;57:49-60.
9. Wu Q, Chi Y, Chen PY, Krauss DJ, Yan D, Martinez A. Adaptive replanning strategies accounting for shrinkage in head and neck IMRT. Int J Radiat Oncol Biol Phys 2009;75:924-32.
10. Barker JL Jr., Garden AS, Ang KK, O'Daniel JC, Wang H, Court LE, et al. Quantification of volumetric and geometric changes occurring during fractionated radiotherapy for head-and-neck cancer using an integrated CT/linear accelerator system. Int J Radiat Oncol Biol Phys 2004;59:960-70.
11. Castadot P, Lee JA, Geets X, Grégoire V. Adaptive radiotherapy of head and neck cancer. Semin Radiat Oncol 2010;20:84-93.
12. Han C, Chen YJ, Liu A, Schultheiss TE, Wong JY. Actual dose variation of parotid glands and spinal cord for nasopharyngeal cancer patients during radiotherapy. Int J Radiat Oncol Biol Phys 2008;70:1256-62.
13. Schwartz DL, Dong L. Adaptive radiation therapy for head and neck cancer-can an old goal evolve into a new standard? J Oncol 2011;2011. pii: 690595.
14. Nath SK, Simpson DR, Rose BS, Sandhu AP. Recent advances in image-guided radiotherapy for head and neck carcinoma. J Oncology 2009;2009:1-10.
15. Chao M, Xie Y, Moros EG, Le QT, Xing L. Image-based modeling of tumor shrinkage in head and neck radiation therapy. Med Phys 2010;37:2351-8.
16. Schwartz DL, Garden AS, Thomas J, Chen Y, Zhang Y, Lewin J, et al. Adaptive radiotherapy for head-and-neck cancer: Initial clinical outcomes from a prospective trial. Int J Radiat Oncol Biol Phys 2012;83:986-93.
17. Delaney G, Jacob S, Barton M. Estimation of an optimal external beam radiotherapy utilization rate for head and neck carcinoma. Cancer 2005;103:2216-27.
18. Chen AM, Daly ME, Cui J, Mathai M, Benedict S, Purdy JA. Clinical outcomes among patients with head and neck cancer treated by intensity-modulated radiotherapy with and without adaptive replanning. Head Neck 2014;36:1541-6.
19. Nishi T, Nishimura Y, Shibata T, Tamura M, Nishigaito N, Okumura M. Volume and dosimetric changes and initial clinical experience of a two-step adaptive intensity modulated radiation therapy (IMRT) scheme for head and neck cancer. Radio- Onco 2013;106:85-9.