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Original Research

# Comparative Evaluation of Octa Shot Versus Quad Shot Palliative Radiotherapy for Advanced Head and Neck Cancer Patients

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**Background and Objective:** The majority of patients with Head and Neck Squamous Cell Cancer in India present at advanced stages, making them unsuitable candidates for multimodality treatment due to loco-regionally advanced disease and poor performance status. Hypofractionated regimens have been used for palliation of advanced head and neck cancers. The purpose of this study was to compare the acute and late toxicity and overall response of octa shot and quad shot radiation therapy as a palliative regimen in locally advanced head and neck cancers.

**Materials and Methods:** This hospital-based prospective, randomized study was conducted with 50 patients with advanced Squamous cell carcinoma of the head and neck, with 25 patients allocated to each treatment arm. Octa shot involved administering two fractions (3.5Gy/#) per day, six hours apart, for four consecutive days. Quad shot involved administering two fractions (3.5Gy/#) per day, six hours apart, for two consecutive days, repeated for one more cycle with a two-week interval. Acute toxicities were monitored at day 15 and 30, and late toxicities were assessed at 3 and 6 months after the treatment initiation.

**Results:** Octa shot demonstrated slightly better loco-regional control, although the difference was not statistically significant. Octa shot resulted in more grade 2 skin and mucosal reactions compared to Quad shot. Symptomatic relief, subjective regression, and improved quality of life were better in the Octa shot group compared to the Quad shot group.

**Conclusion:** Based on the findings of this study, "octa shot" can be an effective palliative radiotherapy regimen with greater yet manageable toxicity compared to the Quad shot regimen. This approach not only can balance the economic burden, treatment time, and machine load, but also can aid in selecting patients for further dose escalation based on treatment response and symptomatic relief. However, further trials with longer follow-up periods and larger sample sizes are required to provide stronger evidence.

## Introduction

Head and neck cancers accounts for almost 2,54,287 new cases annually, among this nearly 60% have non metastatic locally advanced disease [1]. Most of the cancers in developing countries are diagnosed in advanced stages according to the American Joint Committee on Cancer (AJCC 8$^{th}$ edition, 2017) classification and are considered incurable [2]. The goal of the treatment is to palliate symptoms like pain, dysphagia, dyspnea , bleeding, and ulceration and improve quality of life. Radiotherapy (RT) and chemotherapy are the useful modality of treatment for management of advanced head and neck cancer [3]. It is widely recognized that the palliative RT provides effective symptom control and improved quality of life in advanced incurable and metastatic malignancies due to its radiobiological superiority and shorter overall treatment time.

A number of different hypo-fractionated regimens have been used globally for treatment of advanced head and neck cancer [4-5]. Usually these patients are treated with schedule of 30Gy / 10 fractions/ two weeks [6]. The present study was undertaken to compare the efficacy and toxicity of two hypo-fractionated palliative RT regimens in such patients. Comparison of QOL in Octa shot regimen and Quad shot regimen by FACT H & N SCORING SYSTEM.

# Materials and Methods

This was a prospective simple randomized study conducted at Acharya Tulsi Regional Cancer Treatment and Research Institute (ATRCTRI), Sardar Patel Medical College and Associated group of hospitals, Bikaner, Rajasthan.

## Eligibility criteria

The study protocol included 50 patients of biopsy proven previously untreated advanced head and neck cancer who were enrolled from January 2021 to June 2022.

## Inclusion Criteria

1. Surgical unresectable stage IVA, B cancers with poor ECOG score.

2. Age <80year of either sex

3. Adequate baseline hematological, cardiac, renal or liver function tests.

4. Fungating mass of head and neck. Exclusion Criteria

1. Evidence of second malignancy.

2. Prior history of radiotherapy to head and neck region

3. Pregnant or lactating patient

4. Severe stridor at presentation.

The protocol was approved by hospital’s institutional ethical committee, and all patients were properly informed and consented for treatment study. Study design was intent to treat.

Fifty patients who fit the inclusion criteria were randomized into two arms of 25 each, by using the website(http:www.randomisation.com). The arms were

Arm A - Two fractions of 3.5 Gy/# per day atleast six hours apart given in four consecutive days (Octa shot arm). Arm B - Two fractions of 3.5Gy/# per day atleast six hours apart were given in two consecutive days followed by same cycle repeated two weeks later (Quad shot arm).

### Treatment plan

25 patients were planned for an “Octa Shot” schedule, total 28 Gy in eight fractions; 3.5Gy/fr, two such fractions were delivered in four consecutive days, two fractions per day at-least 6 hours apart. The radiotherapy was planned for Cobalt-60 tele-therapy unit, and marking of patients was done around gross tumor volume (primary tumor and involved nodes) with an additional margin of two cm all around. The biologically equivalent dose (BED) for this Octa Shot regimen for tumor and late reacting tissue is 37.8 Gy10 and 60.48 Gy3, respectively. The equivalent dose to 2 Gy/fraction schedule is 31.5 Gy10 for tumor and 36.43 Gy3 for late reacting tissue.

25 patients planned for Quad shot” regime with total 14 Gy in four fractions in two days,3.5Gy/fr, two such fractions per day at-least six hrs apart then same cycle repeated after 14 days. BED of two quad shots is equal to one OCTA shot. After completion of treatment, patients were called for review at 15 days and one month, two months, three months and six months. The assessment of tumor response and toxicity namely mucositis and dermatitis were done according to RECIST criteria and RTOG and CTCAE grading system.

## Results

The baseline patients and tumor characteristics are described in Table 1.

| Characters | Octa-shot group(Arm A) | | Quad-shot group(Arm B) |
|---|---|---|---|
| Age (years) | | | |
| <40 | 3 | | 5 |
| >40 | 22 | | 19 |
| Mean | 54.24 | | 53.52 |
| SD | 10.32 | | 12.26 |
| AJCC Stages | | | |
| Stage IV A | 8 | | 9 |
| Stage IV B | 17 | | 16 |
| Chi square | | 4.051 | |
| P value | | 0.344 | |
| ECOG | | | |
| 0 | 0 | | 0 |
| 1 | 1 | | 1 |
| 2 | 9 | | 11 |
| 3 | 15 | | 13 |
| Chi square | | 0.343 | |
| p value | | 0.842 | |
| Primary site | | | |
| Oral cavity | 6 | | 5 |
| Oropharynx | 15 | | 14 |
| Hypopharynx | 4 | | 6 |
| Chi square | 2.534 | | |
| P value | 0.639 | | |

**Table 1. Patients Characteristics.**

ECOG, Eastern cooperative oncology group; AJCC, American Joint Committee on Cancer

All characteristics were balanced. The treatment response described in Table 2 and the treatment-related toxicities are described in Table 3-4.

| Response | | | Octa Shot Group | | | | | Quad Shot Group | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 weeks | 4 weeks | 2 months | 3 months | 6 months | 2 weeks | 4 weeks | 2 months | 3 months | 6 months | p value |
| PR | 21 | 21 | 17 | 15 | 13 | 22 | 22 | 18 | 16 | 17 | 0.847 |
| CR | 0 | 0 | 4 | 4 | 4 | 0 | 0 | 1 | 1 | 1 | 0.045 |
| SD | 3 | 3 | 1 | 1 | 1 | 3 | 3 | 3 | 3 | 3 | 0.618 |
| PD | 1 | 1 | 2 | 2 | 3 | 0 | 0 | 3 | 3 | 2 | 0.409 |
| Death | 0 | 0 | 1 | 3 | 4 | 0 | 0 | 1 | 2 | 3 | 0.143 |
| TOTAL | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | |

**Table 2. Treatment Response.**

CR, Complete Response; PR, Partial Response; SD, Stable Disease; PD, Progressive disease

| Toxicity | | | Octa Shot Group | | | | | Quad Shot Group | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Skin Reaction | 2 weeks | 4 weeks | 2 months | 3 months | 6 months | 2 weeks | 4 weeks | 2 months | 3 months | 6 months | p value |
| Grade 0 | 0 | 0 | 3 | 12 | 21 | 0 | 0 | 13 | 13 | 22 | 0.0001 |
| Grade 1 | 9 | 8 | 16 | 10 | 0 | 24 | 24 | 11 | 10 | 0 | 0.0001 |
| Grade 2 | 16 | 16 | 5 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0.0001 |
| Grade 3 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.476 |
| Death | 0 | 0 | 1 | 3 | 4 | 0 | 0 | 1 | 2 | 3 | 0.143 |
| Total | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | |

**Table 3. Toxicity Skin (Dermatitis).**

| Toxicity Mucositis | | | Octa Shot Group | | | | | Quad Shot Group | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 weeks | 4 weeks | 2 months | 3 months | 6 months | 2 weeks | 4 weeks | 2 months | 3 months | 6 months | p value |
| Grade 0 | 0 | 0 | 2 | 11 | 21 | 0 | 0 | 15 | 22 | 22 | 0.0001 |
| Grade 1 | 6 | 0 | 15 | 10 | 0 | 10 | 9 | 8 | 1 | 0 | 0.0001 |
| Grade 2 | 17 | 18 | 7 | 1 | 0 | 15 | 16 | 1 | 0 | 0 | 0.0001 |
| Grade 3 | 2 | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.0001 |
| Death | 0 | 0 | 1 | 3 | 4 | 0 | 0 | 1 | 2 | 3 | 0.143 |
| Total | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | |

**Table 4.Toxicity Mucositis.**

21 patients (84%) had an objective response (4 CR,17PR) 1 stable disease, 2 progressive disease and 1 death in Octa shot at 2 months of follow up, In Quad shot 19 patients (76%) had an objective response (1CR,18PR) 3 stable disease, 2 progressive disease and 1 death in Quad shot at 6 months of follow up CR in Octa shot and Quad shot 16% & 4% respectively, which is statistically significant P value (0.045). QOL improved better in Octa shot than Quad shot (Table 2).

Dermatitis was not a significant problem in this study. Most of them had grade 1&2 reaction. Grade I skin toxicity was seen in 9, 8, 16 ,10 patients in Octa Shot &24,24 ,11,10 Quad Shot at 2 weeks, 1 month, 2 months, 3 months and 6 months respectively (p Value=0.0001). Grade 3 skin toxicity in 1 pt in Octa shot vs 0 in Quad shot. (p Value=0.476). Skin toxicities grade 2 &3 more in Octa shot then Quad shot (Table 3).

Majority of the patients developed grade 2 mucositis. 2 patients developed grade 3 mucositis in Octa shot group at weeks 2 and 7 patients at weeks 4 No one developed grade 3 mucositis in Quad

shot. The difference was statistically significant (P value-0.0001).

# Discussion

In this study we compared the acute and late toxicity, overall response and quality of life (QOL) of Octa shot and Quad shot palliative radiotherapy in advanced Squamous Cell Cancers of head and neck by using validated appropriate tools. This study included of fifty consecutive inoperable head and neck cancer patients, who were recruited after getting an informed consent, over a time period of 18 months.

In Octa shot group, 3.5 Gy per fraction, two fraction each day atleast six hours apart were delivered for four consecutive days. In Quad shot group, 3.5 Gy per fraction, two fraction per day atleast six hours apart were delivered for two consecutive days then same cycle was repeated after 14 days interval.

Mean age in Octa shot group was 54.24 years and in quad shot group 53.52 years, in which youngest age 32 year and oldest 79 years old. Patients characteristics like age, TNM staging, primary site, gender, smoking status are similar to previous studies like Lok study, paris et al, Jakhar et al, Mohanti et al, Ghosal et al, Das et al (Table 5).

| Study | Patients | Dose/Fraction (Gy) | Number of fractions | Schedule | Efficacy | Toxicity |
|---|---|---|---|---|---|---|
| Corry et al [7] | 30 | 3.7 BID | 4 | Monthly x 3 | 53% RR 44%Improved QOL | No³Grade 3 toxicity |
| Paris et al [8] | 37 | 3.7 BID | 4 | Monthly x 3 | 77% RR | No late toxicity |
| Monnier et al [9] | 78 | 3 | 8 | Day 1 and 3 Repeated | 54% RR | 31% needed break |
| | | | | weeks 1, 3, 5, 7 cisplatin | | 4% acute grade 3-4 |
| | | | | | | 12% late grade 3-4 |
| Das et al [10] | 33 | 4 | 10 | Twice/Week | 88% Pain Relief60% Improved PS | Grade 3 mucositis 18%Dermatitis 3% |
| Kancherla et al [11] | 33 | 4 | 5 | Repeated after 2 weeks | 7% Symptom Relief72% RR | 18% Grade 3 acute |
| Murthy et al [12] | 505 | 4 | 5 | Additional RT for responders | 37 % RR47%-59% Symptom relief | Not stated for palliative RT |
| Porceddu et al [5] single arm | 37 | 6 | 5-6 | Twice Weekly | 80% RR62% Improved QOL67% Improved pain | Grade 3 mucositis 26%Grade 3 dysphagia 11% |
| Velarasan et al [13] | 64 | 2 | 30-35 | Daily Daily | No differencebetween arms | No difference between arms |
| | | 4 | 10-12 | | | |
| Jakhar et al. [14] | 22 | 3.5 BID | 8 | Daily | 73% RR | 9% Grade 3 Mucositis No Grade 3 dermatitis |
| Neeraj Kumar et al [15] | 60 | 3.5 | 8 | Daily | -- | No Grade 3 Toxicity |
| Ghosal et al [16] | 15 | 3.5 | 8 | Daily | 86% RR | No Grade 3 Toxicity |
| Present Study (Octa Shot V/S | 50 | 3.5 | 8 | Daily | 16 % CR in Octa Shot 4% CR in | Grade 2 Skin Reactions 64 % |

| | | | | | | |
|---|---|---|---|---|---|---|
| Quad Shot) | | | | | Quad Shot 68% PR in Octa Shot 72% PR in Quad Shot | in Octa Shot 4% Quad Shot Grade 3 4% in OctaGrade 3 Mucositis 28% in Octa shot |

**Table 5. Similar Studies of Different Hypo Fractionation Schedules in Head and Neck Cancers.**

BID, twice a day; RR, relative response (CR+PR); QOL, quality of life; PS, performance status; CR, complete response; PR, partial response

In this study, objective response (complete response + partial response) was 84% (21 patients) in Octa shot group and 76% (19 patients) in Quad shot group at two months.

The objective response found in this study is comparable or slightly better than similar previous studies.

Corry et al [l6] and Ghoshal et al have performed studies describing “Quad Shot” in which a short course of palliative radiation 3.5 Gy/fraction is given in four fractions in two days. Such two days regime has shown objective response, i.e., complete and partial response in 53% patients at the end of six weeks. Ghoshal et al. in their study have given two successive “quad shots” to responding patients and have reported partial response in 66.67% patients.

Jakhar et al [14] Octa shot study, first response evaluation at 15 days after the day of treatment started, showed >50 % objective response in 63.33% (14 patients). At one month this objective response increased to >75 % in 73% (16 patients) and 50%-75% in 13.63% (three patients).

In this study grade 2 mucositis was developed in majority of cases, as 72 % patients in Octa shot group and 64 % patients in Quad shot group patients. Grade 3 mucositis developed in Octa shot group 28% but none in Quad shot group.

Majority of patients developed grade 1 and 2 skin toxicity in Octa shot group but in Quad shot group majority of patients developed grade 1 skin toxicity. Grade 3 skin toxicity developed in only one patient in Octa shot group, these toxicities are comparable with previous studies.

Previous studies have concluded that due to palliative nature of the treatment, late tissue toxicities were not a significant problem in the patients received short course palliative radiotherapy. So, patients received further radiotherapy did not have any worst late toxicity as compared to patients received initial palliative radiotherapy alone.

In this study QOL measured by FACT H& N, QOL improved better in Octa shot group then Quad shot group but statistically insignificant.

Mean FACT H& N TOI observed in Octa shot group before radiotherapy was 58.92 with SD 7.95 and in Quad shot 56.54 with SD 8.06. After 3 months of radiotherapy in Octa shot mean FACT H&N TOI were 64.92 with SD 13.95 and in Quad shot mean 60.54 with SD 12.06.

Mean FACT -G TOTAL SCORE in Octa shot group before radiotherapy were 63.05 with SD 8.33 and in Quad shot group 58.77 with SD 12.00. After 3 months of radiotherapy Mean FACT-G TOTAL SCORE in Octa shot 69.05 with SD 14.33 and in Quad shot 62.77 with SD 16.00.

Mean FACT H&N TOTAL SCORE in Octa shot group before radiotherapy were 90.18 with SD 10.91 and in Quad shot 86.35 with SD 13.92. After 3 months of radiotherapy Mean FACT H&N TOTAL SCORE 98.18 with SD 18.91 and in Quad shot group 92.35 with SD 19.92.

In conclusion, Octa shot is an effective palliative radiotherapy regimen with greater yet manageable toxicity in comparison to Quad shot regimen. This regime not only strikes a balance between the economic burden, treatment time, machine load but also helps in selecting patients for further dose escalation based on treatment response and symptomatic relief. However more such trials with longer follow up and larger sample size are required for stronger evidences.

# References

# References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International Journal of Cancer.* 2015; 136(5)DOI
2. Nath A, Sathishkumar K, Das P, Sudarshan KL, Mathur P. A clinicoepidemiological profile of lung cancers in India - Results from the National Cancer Registry Programme. *The Indian Journal of Medical Research.* 2022; 155(2)DOI
3. Joshi P, Dutta S, Chaturvedi P, Nair S. Head and neck cancers in developing countries. *Rambam Maimonides Medical Journal.* 2014; 5(2)DOI
4. Chen AM, Vaughan A, Narayan S, Vijayakumar S. Palliative radiation therapy for head and neck cancer: toward an optimal fractionation scheme. *Head & Neck.* 2008; 30(12)DOI
5. Porceddu SV, Rosser B, Burmeister BH, Jones M, Hickey B, Baumann K, Gogna K, Pullar A, Poulsen M, Holt T. Hypofractionated radiotherapy for the palliation of advanced head and neck cancer in patients unsuitable for curative treatment--"Hypo Trial". *Radiotherapy and Oncology: Journal of the European Society for Therapeutic Radiology and Oncology.* 2007; 85(3)DOI
6. Adlakha P, Maheshwari G, Dhanawat A, Sinwer R, Singhal M, Jakhar SL, Sharma N, Kumar HS. Comparison of two schedules of hypo-fractionated radiotherapy in locally advanced head-and-neck cancers. *Journal of Cancer Research and Therapeutics.* 2022; 18(Supplement)DOI
7. Corry J, Peters LJ, Costa ID, Milner AD, Fawns H, Rischin D, Porceddu S. The 'QUAD SHOT'--a phase II study of palliative radiotherapy for incurable head and neck cancer. *Radiotherapy and Oncology: Journal of the European Society for Therapeutic Radiology and Oncology.* 2005; 77(2)DOI
8. Paris KJ, Spanos WJ, Lindberg RD, Jose B, Albrink F. Phase I-II study of multiple daily fractions for palliation of advanced head and neck malignancies. *International Journal of Radiation Oncology, Biology, Physics.* 1993; 25(4)DOI
9. Monnier L, Touboul E, Durdux C, Lang P, St Guily JL, Huguet F. Hypofractionated palliative radiotherapy for advanced head and neck cancer: the IHF2SQ regimen. *Head & Neck.* 2013; 35(12)DOI
10. Das S, Thomas S, Pal SK, Isiah R, John S. Hypofractionated Palliative Radiotherapy in Locally Advanced Inoperable Head and Neck Cancer: CMC Vellore Experience. *Indian Journal of Palliative Care.* 2013; 19(2)DOI
11. Kancherla KN, Oksuz DC, Prestwich RJD, Fosker C, Dyker KE, Coyle CC, Sen M. The role of split-course hypofractionated palliative radiotherapy in head and neck cancer. *Clinical Oncology (Royal College of Radiologists (Great Britain)).* 2011; 23(2)DOI
12. Murthy V, Kumar DP, Budrukkar A, Gupta T, Ghosh-Laskar S, Agarwal J. Twice-weekly palliative radiotherapy for locally very advanced head and neck cancers. *Indian Journal of Cancer.* 2016; 53(1)DOI
13. Velarasan SK, Ramasundaram D. Palliative hypofractionated radiation therapy in incurable head-and-neck cancer patients–2-year follow-up experience from a tertiary center from South India. *Journal of Radiation and Cancer Research. 2022.* 2022; 13(2):60.
14. Jakhar SL, Purohit R, Solanki A, Murali P, Kothari T, Sharma N, Kumar HS. Accelerated hypofractionation (OCTA SHOT): Palliative radiation schedule in advanced head and neck carcinoma. *Journal of Cancer Research and Therapeutics.* 2017; 13(6)DOI

15. Kumar N, Atri R, Kaushal V, Dhankhar R, Dhull A, Gupta P, Bhardwaj S, Mukutawat P. Comparative Evaluation of Quad Shot versus Twice Weekly Palliative Radiotherapy for Locally Advanced Head and Neck Cancer. *Journal of Evidence Based Medicine and Healthcare.* 2020; 7DOI
16. Ghoshal S, Chakraborty S, Moudgil N, Kaur M, Patel FD. Quad Shot: A Short but Effective Schedule for Palliative Radiation for Head and Neck Carcinoma. *Indian Journal of Palliative Care.* 2009; 15(2)DOI