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Prospective study of sequential volumetric changes of parotid gland in early oropharyngeal carcinoma patients treated by intensity-modulated radiation therapy: An institutional experience

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Abstract

Aims and Objectives: During course of radiation therapy, anatomical variations occur risking overdose of parotid gland. We tried to quantify volume of parotid gland and mean dose to parotid gland after every 10 fractions (#). **Materials and Methods:** We conducted the prospective study from July 2016 to May 2017 in 25 patients of early-stage oropharyngeal carcinoma. Patients had Karnofsy Performance Score of 80–100, median age was 54 years, and 18 patients were males. Patients were planned with intensity-modulated radiation therapy planning with dose as 66 Gy/30# to planning target volume (PTV) including primary and 54 Gy/30# to PTV-nodal including elective neck irradiation. After each 10#, replanning was done, and variations in parotid volume were studied including D_{mean} (mean dose to parotids) and D_{50} (the dose delivered to 50% of volume). Other tumor characteristic like PTV of primary was also assessed and minimum PTV volume covered by 95% isodose line was kept as 95%. **Results:** Average parotid volumes decreased by the mean value of 10% and 6% for the left and right parotids, respectively, and PTV of primary target decreased by mean of 13%. The difference in D_{mean} doses to parotid glands was 32% and 42% and difference in D_{50} dose was 30% and 35% on the left and right side, respectively. **Conclusions:** The parotid volumes differ considerably during adaptive planning done after every ten fractions. These differences in parotid volumes and doses received to parotid glands play a significant role in the risk of xerostomia observed during later follow-up.

Key words: Intensity-modulated radiation therapy, oropharyngeal carcinoma, parotid gland

Introduction

The head and neck malignancies constitute 5% of all the cancers globally. The geographic distribution of head and neck cancers reflects huge variation for different countries and regions. The most common head and neck cancers are those of oral cavity and pharynx in India. In males, oral and pharyngeal carcinomas rank third most common cancers, whereas, in females, these oral and pharyngeal carcinomas rank as fourth.

The treatment of oropharyngeal malignancies is radiotherapy with good control rates, especially for early staged oropharyngeal carcinomas where the 5-year survival rates are 60%–80%. However, since oropharyngeal region is important for functions such as swallowing and speech, radiotherapy treatment can lead to good control rates but affecting patient's quality of life significantly. The most common toxicity is xerostomia[1] affecting the quality of life including difficulty in swallowing and speaking, loss of taste, and dental caries. The main reason of xerostomia is damage caused to parotids mainly and to lesser extent submandibular glands and minor salivary glands by radiation. Conformal techniques such as intensity-modulated radiotherapy (IMRT) help delivery high dose to target volumes conformally and at the same time sparing critical structures. The PARSPORT trial also documented advantage of parotid sparing with IMRT[2] as compared to non-IMRT techniques. Pow *et al*.[3] and Kam *et al*.[4] also showed the advantage of parotid sparing with IMRT techniques, thereby improving quality of life of patients. It is of paramount importance to use conformal treatment strategies keeping in mind high cure rates with minimal acute and especially late toxicities. Despite the advantage of conformal techniques such as IMRT, there is still huge variation in the target volumes and parotid glands in concordance with tumor shrinkage, parotid gland volume reduction, weight loss, and edema fluctuation, especially in postoperative head and carcinoma cases.[5-7]

Thus, the concept of adaptive radiotherapy[8,9] which is basically changing the radiation treatment plan during the course of radiotherapy treatment in accordance with changes in tumor shrinkage, weight loss, and edema fluctuation was introduced. It is a very effective solution so as to ensure proper conformal dose to the target region and minimizing toxicities of radiation treatment.

Materials and Methods

We conducted a prospective study from July 2016 to May 2017 approved by the Institutional Review Board and Ethics Committee of the institute in 25 patients of early-stage oropharyngeal carcinoma (T1, T2, N0, and M0). Patients were investigated and planned according to the institute's routine practice including routine blood investigations, chest X-ray, computed tomography (CT) scan head and neck, direct laryngoscopy, and biopsy. The inclusion criteria included patient's age <70 years, Karnofsky Performance Scale (KPS) score 80–100, newly diagnosed histologically proven squamous cell carcinoma of Stage I and II (T1, T2, N0, and M0) oropharynx with thorough proper workup. The exclusion criteria included the previous history of radiotherapy in head and neck region. All patients were immobilized with head and neck orfit with 5 clamps, and CT scan with 3 mm slice was done from skull to carina level. The target

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volume seen clinically and radiologically was named as gross target volume to which margin of 10 mm was added three-dimensionally to form clinical target volume (CTV) taking into account the microscopic avenues of spread. Finally, another 5 mm margin was added to CTV to form finally planning target volume (PTV) taking into account the set-up uncertainties. The PTV here mentioned includes both the primary and PTV nodal (PTV-N) including elective neck irradiation.

All patients were treated with IMRT plans with replanning CT scan done after every ten fractions (#) of treatment. There were total three plans made during the course of treatment (Plan 1 – CT 1, Plan 2 after 10#-CT 2, and Plan 3 after 20#-CT 3). After each 10# as a part of adaptive planning, replanning was done, and variations in parotid volume were studied including D_{mean} (mean dose to parotids) and D_{50} (the dose delivered to 50% of the volume). Other tumor characteristic like PTV of primary was also assessed, and the minimum PTV volume covered by 95% isodose line was kept as 95%. These dosimetric variables were calculated for each 10# and their mean values taken for each patient. The radiotherapy dose was kept as 66 Gy/30# to PTV including primary and 54 Gy/30# to PTV-N including elective neck irradiation. The other dose volume constraints for organs at risk were according to QUANTEC recommendations such as (Spinal cord D_{max} <45 Gy, brainstem D_{max} <54 Gy, temporomandibular joint D_{max} <60 Gy, inner ear D_{max} <60 Gy, parotid mean dose D_{mean} <26 Gy, parotid gland V_{30} <50%, oral cavity V_{40} <30%, larynx-oesophagus-trachea V_{40} <30%, optic nerve D_{max} <54 Gy, and lens D_{max} <5 Gy).

Results

The median age of presentation was 54 years (48–67 years), and 18 patients were males. The median KPS score was 90. The tumor characteristics in terms of parotid volumes for both ipsilateral and contralateral parotid glands mean dose to parotid glands (Dmean), dose to 50% of parotid volumes (D_{50}), and primary PTV volume are shown below in Table 1. These tumor characteristics were calculated for each 10#, and first, the mean values of all variables – left and right parotid gland volumes, primary target volumes, D_{mean} dose to the left and right parotids, and D_{50} dose to the left and right parotids were calculated for each patient and then the mean of all the variables was calculated for the whole population which is shown in Table 1.

Statistical analysis

All these data were analyzed in Microsoft excel and EPT INFO 7.0 software. As it was quantitative data with three groups, we have used analysis of variance test with 95% confidence interval. These variables with their statistical significance are given in Table 1.

As seen in Table 1 above, we observed 13% (average of difference from CT 1 to CT 2 and from CT 1 to CT 3) decrease in primary target volume (P < 0.01) and 10% and 6% decrease in parotid volumes of left and right parotid glands, respectively (P < 0.01, both sides).

Due to the differences in the primary target volume as well as parotid glands volume, we could appreciate difference in D_{mean} doses (mean dose to parotid glands) to the parotid glands (P < 0.01, both sides), average as 32% and 42% on the left and right side, respectively (average of difference from CT 1 to CT 2 and from CT 1 to CT 3). The difference in D_{50} dose (dose to the 50% volume of the parotid glands) was 30% and 35% on the left (P < 0.0001) and right side (P < 0.01), respectively (average of difference from CT 1 to CT 2 and from CT 1 to CT 3).

Discussion

There is paradigm shift from conventional radiation to conformal radiation in the past three to four decades mainly due to interest in sparing the critical structures, and at the same time, dose escalation to the tumor area. The main advantage of parotid gland sparing from IMRT treatment to avoid the most important complication of xerostomia from radiation has made IMRT, the standard treatment for head and neck cancers. However, there is a lot of variation in dose to parotid gland[10] from tumor shrinkage and weight loss, resulting in an unanticipated overdose to the parotids. Parotids being the main drive for saliva production have become a matter of interest to spare possible through replanning during the radiation treatment known as adaptive radiotherapy.[11] Replanning during radiation therapy can correct these anatomical changes and protect parotid glands from an overdose of irradiation. However, the indications and timing and replanning are still a big matter of debate, and there are no clear guidelines till date.[12-14]

We conducted a prospective study from July 2016 to May 2017 approved by the Institutional Review Board of institute and Ethics Committee in 25 patients of early-stage oropharyngeal carcinoma (T1, T2, N0, and M0). After proper workup, these patients were taken for IMRT treatment. Realizing the potential of conformal therapies to reduce toxicities most importantly xerostomia and also the fact that still, huge parotid gland variations occur during the course of radiation treatment, adaptive radiotherapy was intended with

Table 1: Patient tumor and treatment characteristics at the initial planning (CT 1, first replanning after 10#-CT 2 and second replanning after 20#-CT 3). Mean of all variables of each patient taken and then the mean of whole population

Parameters	CT 1	CT 2 (%)	CT 3 (%)	Difference (P)
Parotid volumes-left (cc)	21	19.5 (7)	18 (14)	10% (<0.01)
Parotid volumes-right (cc)	24	23.5 (2)	21.5 (10)	06% (<0.01)
D_{mean} - left (Gy)	11	9 (18)	6 (45)	32% (<0.01)
D_{mean} - right (Gy)	12	9 (25)	5 (58)	42% (<0.01)
D_{50} - left (Gy)	13	10 (13)	7 (46)	30% (<0.0001)
D_{50} - right (Gy)	14	11 (12)	6 (57)	35% (<0.01)
Primary PTV volume (cc)	201	185 (8)	165 (18)	13% (<0.01)

PVT=Planning target volume, CT=Computed tomography replanning after every 10#. Till date, with no literature having clear guidelines on a number of replanning and indications and also because of financial reasons and a huge workload, we decided to go for replanning after every 10# thus in total there were two replanning CT scans done during the radiation treatment.

Our study showed the difference in D_{mean} doses (mean dose to parotid glands) to the parotid glands, average as 32% and 42% on the left and right side, respectively (average of difference from CT 1 to CT 2 and from CT 1 to CT 3). This difference was statistically significant ($P < 0.01$, both sides) signifying that unanticipated overdose to the parotids could be avoided due to replanning. The difference in D_{50} dose (dose to the 50% volume of the parotid glands) was 30% and 35% on the left ($P < 0.0001$) and right side ($P < 0.01$), respectively (average of difference from CT 1 to CT 2 and from CT 1 to CT 3) stating that this difference was also statistically highly significant. These differences in D_{mean} doses and D_{50} doses are attributed because of tumor shrinkage (decrease of 13% which is average of difference from CT 1 to CT 2 and from CT 1 to CT 3) decrease in primary target volume, $P < 0.01$, statistically significant) and associated variations in parotid gland volumes (10% and 6% decrease in parotid volumes of the left and right parotid glands, respectively, $P < 0.01$, both sides statistically significant).

The initial results of our study showed significant changes in parotid volumes during radiotherapy treatment, and this can be a good reason and justification to do adaptive replanning, thereby preventing unanticipated high dose to the parotid. We expect such changes also in advanced cases where in fact the tumor shrinkage would be more significant leading to indirect changes in parotid volume and thus effect on dose to parotid glands as well.

Adaptive replanning should be employed as standard practice to decrease rates of xerostomia and thus helping to improve the quality of life more in cases treated with conformal techniques such as IMRT.

Conclusions

Our study showed considerable differences in the parotid volumes during adaptive planning after every ten fractions of radiotherapy. Due to reasons including financial and heavy workload, we had two replannings done in our protocol still the results displayed appreciable differences in parotid volumes preventing high doses to parotid glands. These results of parotid glands getting protected from overdose would play a significant role in the risk of xerostomia observed during later follow-up. We strongly advocate the use of adaptive replanning in head and neck cancers; however, the protocol should be individualized according to the centers as well as the disease site and stage.

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Conflicts of interest

There are no conflicts of interest.

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