

CORRELATION OF LOCAL RECURRENCE IN ORAL SQUAMOUS CELL CARCINOMA WITH TUMOR SIZE AND DELAY IN POSTOPERATIVE ADJUVANT RADIATION

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Abstract

Objective: "To determine the correlation of local recurrence in oral squamous cell carcinoma with tumor size and delay in postoperative adjuvant radiation"

Study Design: Descriptive study

Study place and Duration: Department of Oral and Maxillofacial Surgery, University of Lahore, Lahore from Feb 2024 to July 2024

Methodology: After meeting the selection criteria total 62 confirmed patients oral squamous cell carcinoma were enrolled. Informed consent and demographic detail was taken. After surgery patients were followed up for 1 years. The initiation of radiotherapy was noted and labeled delayed as per criteria discussed above. Patients were advised for routine follow up visits. During follow-up if local recurrence observed. All the data was collected on pre-designed proforma.

Results: In this study regarding outcomes, recurrence occurred in 12 (34.3%) patients who received delayed postoperative radiation, compared to 1 (3.8%) patient without delayed radiation, showing a statistically significant association between delayed radiation and cancer recurrence ($p = 0.004$). Additionally, the mean postoperative tumor size was significantly larger in patients with recurrence (31.92 ± 9.78 mm) than in those without recurrence (22.42 ± 16.07 mm) ($p = 0.012$).

Conclusion: It has been concluded that tumor size and delay in postoperative adjuvant radiation are significantly associated with local recurrence of oral

INTRODUCTION

Knowing the primary and nodal Clinical Target Volumes (CTVs) for radiotherapy in the context of oral cavity squamous cell carcinoma (OCSCC), which is usually treated by surgery followed by post-operative radiotherapy, is crucial to the practice of head and neck radiation and clinical oncologists¹. The sub-entity of squamous cell carcinoma of the oral cavity (OSCC) causes around 300,000 cases and 145,000 deaths annually globally, whereas head and neck squamous cell carcinoma (HNSCC) is the sixth most prevalent cancer overall².

Oral squamous cell carcinoma (OSCC) frequently has tumor recurrence³. About 20% of instances of OSCC return after primary curative therapy, with 76% of recurrences occurring within the first two years³. According to reports, 30% of patients who had recurrence survived⁴. The survival percentage for local recurrence is 66.7%. SPTs start as precursor lesions of the oral mucosal epithelium, whereas local recurrences are brought on by cancer cells that remain after surgery. The most frequent recurrence pattern in individuals who had OSCC surgically removed alone is regional (50%), followed by local (38.9%) and loco-regional (13%) recurrences⁵.

These days, lymph node metastasis, tumor size, and resection status are the most prevalent prognostic variables for overall survival and tumor recurrence^{6,7}. On the other hand, there is debate regarding the relationship between histopathological grade and overall and disease-free survival. Histopathological grading is proven to have limited prognostic utility, particularly for early tumor stages⁸.

For patients with head and neck cancer, postoperative radiation treatment is typically recommended when recurrence risk is high. Radiation therapy should ideally start six weeks following surgery. Adjuvant radiation therapy's therapeutic impact is diminished if it is started later because the scarred tissue becomes hypoxic and tumor cells repopulate⁹. Approximately 26% of OSCC patients relapse after receiving initial curative therapy, with over 80% of these

recurrences taking place within the first two years, according to earlier research. As a result, delayed local recurrences (DLR) in OSCC patients that happen after two years are rare¹⁰.

The primary treatment for oral squamous cell carcinoma is surgery; alternative treatments include radiation therapy, chemotherapy, or targeted therapy to prevent recurrence. It is thought that waiting and treatment together make up more time than waiting alone, and that expedited radiation therapy regimens might make up for a delay⁹. As per our knowledge there is no study has been done previously in our local population on this topic. This study was designed to ascertain the relationship between tumor size and postoperative adjuvant radiotherapy delay and local recurrence in oral squamous cell carcinoma.

METHODOLOGY

After approval from institutional review board, this descriptive study was carried out at Department of Oral and Maxillofacial Surgery, University of Lahore, Lahore from Feb 2024 to July 2024. Calculated sample size for this study was 62 using 20% local recurrence rate after the primary curative treatment of OSCC³. For this study calculation the level of significance was 5% and margin of error was 10%. All the cases were enrolled by applying non-probability consecutive sampling technique.

Inclusion criteria: The cases having age range between 18 to 80 years of both gender presented with oral squamous cell carcinoma of tongue confirmed on histopathology were fall in inclusion criteria.

Exclusion criteria: Patients with neoadjuvant chemo or radiotherapy before the surgery and patients lost to follow up were fall in exclusion criteria.

On initial evaluation informed consent and demographic information like age, gender, tumor size etc were noted. Patients were evaluated for OSCC surgery was performed and patients were advised for radioactive treatment. Patients were

followed up for 1 years. The initiation of radiotherapy was noted and labeled delayed. Delayed radiation after the surgical treatment of the patients was labeled if patients had duration of delayed radiation >6 weeks. Patients were advised for routine follow up visits. During follow-up if local recurrence was observed then it was noted and treated the patients as per standard protocol. Local recurrence was labeled if patients have the return of disease at same location where originally appeared. All the information was collected on predesigned Proforma.

All the collected data was entered and analyzed on SPSS version 26. To assess the relationship between the local recurrences with delayed initiation of radiotherapy Chi square test was applied. $P\text{-value} \leq 0.05$ was taken as significant. Independent sample t-test was applied between the comparison of local recurrence and tumor size of the patients. $P\text{-value} \leq 0.05$ was taken as significant.

RESULTS:

In this study, a total of 62 patients with OSCC were enrolled. The mean age of the patients was 48.79 ± 8.46 years. In this study, the majority of patients were male, comprising 58 (93.5%) cases. The mean BMI was 18.57 ± 0.96 kg/m², the average duration of cancer was 8 ± 0.15 months, and the mean postoperative tumor size was 24.32 ± 15.29 mm. A total of 32 (51.6%)

patients belonged to urban areas, while 30 (48.4%) were from rural areas. Among the comorbidities, diabetes mellitus was observed in 12 (19.4%) patients, hypertension in 10 (16.1%), smoking in 39 (62.9%), and tobacco use in 26 (41.9%) patients. A positive family history of cancer was reported in 8 (12.9%) patients. **Table 1**

The tumor was located on the left side in 42 (67.7%) patients. Unilateral neck dissection was performed in 52 (83.9%) patients, whereas bilateral neck dissection was done in 10 (16.1%) patients. Histopathological evaluation revealed well-differentiated tumors in 11 (17.7%) patients. With respect to outcome variables, delayed postoperative radiation was noted in 35 (56.5%) patients, and local recurrence was observed in 13 (21.3%) patients. **Table 2**

In terms of outcome recurrence was observed in 12 (34.3%) patients who experienced delayed postoperative radiation, compared to 1 (3.8%) patient without delayed radiation. This difference demonstrated a statistically significant association between delayed radiation and cancer recurrence ($p = 0.004$). Furthermore, the mean postoperative tumor size among patients with recurrence was 31.92 ± 9.78 mm, whereas in patients without recurrence it was 22.42 ± 16.07 mm. This difference was also statistically significant ($p = 0.012$). **Table 3**

Table 1: Descriptive statistics of quantitative variables of the patients (n = 62)

	Mean
Age (Years)	48.79 ± 8.46
Gender	
Male	58 (93.5%)
Female	4 (6.5%)
BMI (Kg/m ²)	18.57 ± 0.96
Duration of cancer (months)	8.00 ± 5.15
Preoperative size of tumor mm	24.32 ± 15.29
Residence	
Urban	32 (51.6%)
Rural	30 (48.4%)
Occupation	
Carpenter	2 (3.2%)

Constructor	2 (3.2%)
Farmer	6 (9.7%)
Govt.	4 (6.5%)
Housewife	4 (6.5%)
Labour	9 (14.5%)
Painter	1 (1.6%)
Plumber	4 (6.5%)
Private	17 (27.4%)
Salesman	2 (3.2%)
Shopkeeper	9 (14.5%)
Sweeper	2 (3.2%)
History of	
Diabetes	12 (19.4%)
Hypertension	10 (16.1%)
Smoking	39 (62.9%)
Tobacco Use	26 (41.9%)
FH of cancer	8 (12.9%)
Alcoholism	4 (6.5%)

Table 2: Descriptive statistics of clinical characteristics patients (n = 62)

		F (%)
Site of tumor	Left	42 (67.7%)
	Right	20 (32.3%)
Stage of cancer	Two	2 (3.2%)
	Three	16 (25.8%)
	Four	44 (71.0%)
Neck Dissection	Unilateral	52 (83.9%)
	Bilateral	10 (16.1%)
Cell differentiation on histopathology	Well differentiated	11 (17.7%)
	Moderately	40 (64.5%)
	Poorly Differentiated	11 (17.7%)
Tumor Margin	Closed	31 (50%)
	Distinct	31 (50%)

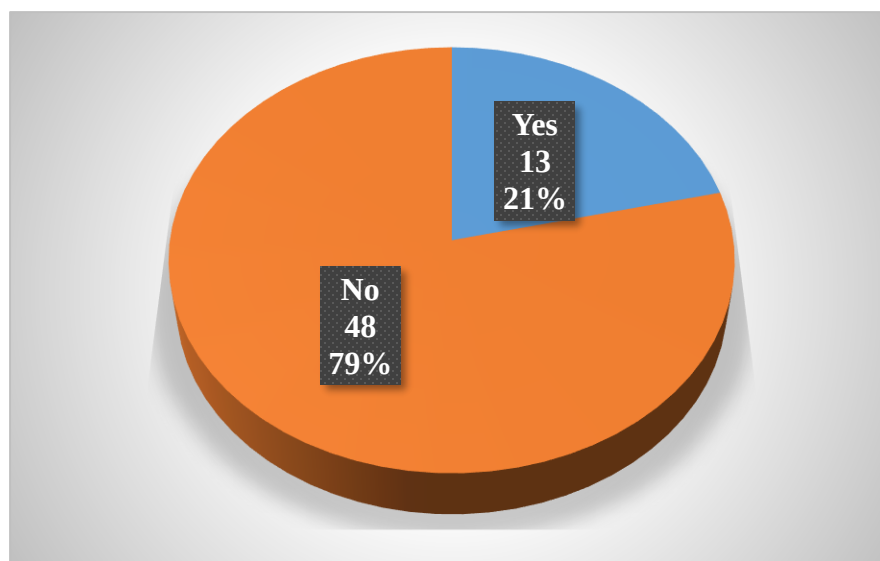


Figure 1: Recurrence observed in the whole sample (n = 62)

Table 3: Comparison of recurrence between delayed post-op radiation and post-op size of tumor (mm)

			Recurrence		Total	p-value
			Yes	No		
Delayed post-op radiation	Yes		12 (34.3%)	23 (65.7%)	35 (56.5%)	0.004
	No		1 (3.8%)	25 (96.2%)	27 (43.5%)	
Post-op size of tumor (mm)			31.92 ± 9.78	22.42 ± 16.07	~	0.012

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DISCUSSION:

The most prevalent cancer in the head and neck area is oral squamous cell carcinoma. According to estimates from 2018, oral carcinoma causes over 177,000 deaths worldwide each year. Due to addictions like pan, chaliya, and gutka, this illness is far more common in the subcontinent, particularly in Karachi¹¹⁻¹³. Furqan Mirza et al presented the same findings observed in our study. The author reported that local recurrence rate was 0% in T1, 8.6% in T2, 19.1% in T3 and 40.0% in T4 lesions (p-value = 0.001), 1.6% where safe margin is > 10 mm, 34.7% where margins are between 1 to 5 mm and 100% where < 1 mm (p-value = 0.002). Similarly recurrence rate was 5.5% when adjuvant radiation started within 1 month, 4.8% when started between 1 to 3 months, 30.4% when between 3 to 6 months and 78.5% when started > 6months after primary surgery (p-value = 0.001)¹¹. Similarly Naomi Rahman et al also concluded that high risk'

tumours were significantly associated with distant metastasis possibly due to the greater likelihood of aggressive features such as WPOI and PNI. Primary tumours are more likely to express high risk features with increasing T stage. None of the patients classified as 'low risk' died perhaps suggesting these tumours represent a rare variant of OSCC with excellent prognosis¹².

A study by Tasche et al showed that only significant margin involvement for recurrence is important if it is less than 1 mm.²¹ While a study by Zanoni et al showed that recurrence rate is higher only if the resected margins for tumour is < 2.2 mm^{14, 15}. One more study documented that Delay in initiation of adjuvant radiotherapy is defined as start of radiotherapy more than 6 weeks after the primary surgery. This delay in adjuvant radiotherapy is one of the important

reason for higher recurrence rate both at the primary site and in cervical nodes ¹⁶. Another study presented that there is a higher proportion of patients having radiotherapy had loco-regional recurrence (19/80 24%) compared to those treated by surgery alone (17/113 15%). The improved salvage rate for recurrent disease in the surgery alone group (8/17 53%), compared to those receiving radiotherapy (2/19 13%, $P=0.05$), indicates an advantage in withholding radiotherapy for patients at intermediate risk of recurrence ¹⁷.

A study by A Amar et al As a consequence, 54 individuals (35%) received a diagnosis of local recurrence. While not statistically significant, radiation treatment decreased the rate of local recurrences. For patients referred for adjuvant treatment, the interval between surgery and the start of postoperative radiation had no discernible impact on the likelihood of local recurrence ($p=0.49$) ⁹.

A study done by E.A Dik et al. ofound that individuals without adjuvant therapy who had margins between 3-6 mm and those with distant margins (> 6 mm) did not significantly vary in their local recurrence rates. Additionally, their study lacked statistical power to provide sufficient data to support their suggestion that re-resection is a superior alternative for narrow margins less than 3 mm ¹⁸. Zanoni et al. set a cutoff limit of 2.2 mm, below which the oncological result is poorer ¹⁹.

CONCLUSION:

This study concludes that tumor size and delay in postoperative adjuvant radiation are significantly associated with local recurrence of oral squamous cell carcinoma

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