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Research Article

Comparative Analysis of rates of Local Recurrence with different Margin Dimensions in Oral Squamous Cell Carcinoma.

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Introduction

Oral squamous cell carcinoma is one of the most common malignancies. Surgical resection is the mainstay of treatment. Any adjuvant radiotherapy or chemotherapy is administered in case of presence of any adverse factors. Out of all risk factors, positive or close margin has proven to be one of the major high-risk factors [1,2]. The National Comprehensive Cancer Network (NCCN) has therefore stated positive or close margin as clear indication for administering adjuvant chemoradiotherapy [3]. The most adequate dimension for a clear margin is said to be 5mm as per multiple studies [4]. There are many factors responsible for achieving an adequate margin intraoperatively, such as, use of cautery, prior radiotherapy, disease stage, surgical techniques etc [5].
The use of frozen section technique has been considered very useful in achieving adequate margins by many institutes. Although frozen section is considered to have a high specificity for clear margins but the sensitivity to detect positive margins is still considered low according to some studies [6-9]. NCCN guidelines recommends usage of specimen-based sampling than patient based sampling [3]. Frozen section has remained as one of the most used methods to determine final margin status. Although numerous studies have showed that re-resection of surgical margin based on frozen section reports doesn't imply a better local recurrence free survival (LRFS) [10-14].

The use of frozen section can be effective in achieving negative margins in many number of cases but it is not cost effective and doesn't eradicate the chances of a positive or close margin in the final histopathology report. Since it is technically difficult to assess the margin all around the tumour, hence representative areas around the lesion are chosen and examined. Thus, it explains the rate of local recurrences despite negative margins on frozen section. Studies also suggests that there can always be a discrepancy between the close margins stated by the pathologists in the specimen side and the actual re-resection done by the surgeon on the patient side which again proves the rate of local recurrence even with the usage of frozen section.
Despite all the usefulness of frozen section, it still has a poor cost-benefit ratio. Considering the high cost and high technical requirements of frozen section, it is not vastly used in all centres.
In this study, we aim at identifying the rate of local recurrence in direct relation with the margin as per the final histopathological reports. It should be noted that frozen section technique was not used intraoperatively in these patients. We performed a observational study on patients to quantify the effect of each margin group on 2 year local recurrence free survival.

Materials and Methods

An observational retrospective cohort study was performed on 100 patients operated for oral squamous cell carcinoma between September 2019 to September 2021. All these patients were de novo cases of oral squamous cell carcinoma diagnosed on biopsy and none of them had received any neo-adjuvant therapy. The patients underwent surgical resection of the primary tumor with an elective neck dissection. All the patients received adequate adjuvant radio or chemotherapy as per their final histopathological reports according to the NCCN guidelines. It is worth noting that frozen section techniques were not used intraoperatively in any of the study participants.

All these patients were followed up for two years for local recurrence free survival (LRFS). The results of 6 month, 12 month and 2 year LRFS was documented. The rate of local recurrence at 6,12 and 2 year periods were analysed as per their margin statuses. The relationship between the particular margin dimension and the earliest time of recurrence was established as per the follow up data obtained.

Inclusion criteria

1) Oral squamous cell carcinoma
2) Patients who have not received any neo adjuvant therapy.
3) Patients who had not been operated before.
4) Patients who followed up for two years in regular intervals.
5) Patients with operable tumors

Exclusion criteria

1) Patients who have been operated before.
2) Patients who have received chemo or radiotherapy before.
3) Patients who were lost to follow up.

The data collected with follow up of 2 years was tabulated and final relationship between specific margin and local recurrence were established.

Results

A total of 100 patients were included in the analysis. The primary end point of the study was to establish rate of local recurrence with every decrease in dimension of margins. At final analysis, out of 100 patients, the prevalence of different margins were, 1 mm was seen in 2 patients (2%), 2 mm seen in 14 patients (14%), 3 mm was seen in 9 patients (9%), 4 mm was seen in 14 patients (14%), and 5mm or more was seen in 61

patients (61%).

Margin dimension	No. of patients
1mm	02
2 mm	14
3 mm	09
4 mm	14
≥ 5 mm	61
Total	**100**

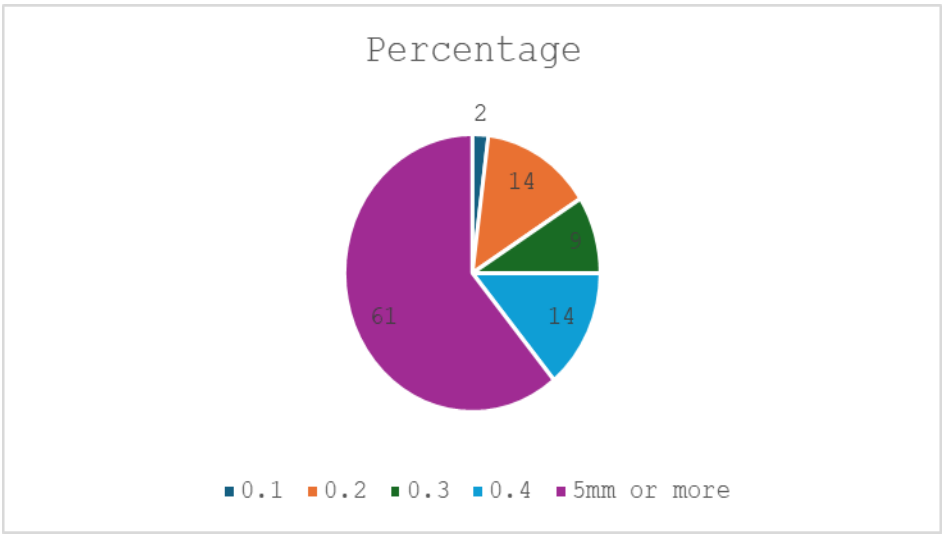

Fig 1

Out of all patients who had 1mm margins (2%), 100% (n=2) patients got local recurrence, patients with 2 mm margins (14%), 21 % (n=3) patients got local recurrence, patients with 3 mm margins (9%), 44% (n=4) patients got local recurrence, patients with 4 mm margins (14%), 7 % (n=1) got local recurrence. Among all patients with adequate margins (i.e, ≥ 5mm) (61%), 8 % (n=5) got a local recurrence.

	No. of patients	Recurrence	Percentage
1 mm	02	02	100 %
2 mm	14	03	21 %
3 mm	09	04	44 %
4 mm	14	01	07 %
≥ 5mm	61	05	08 %
Total	100	15	--

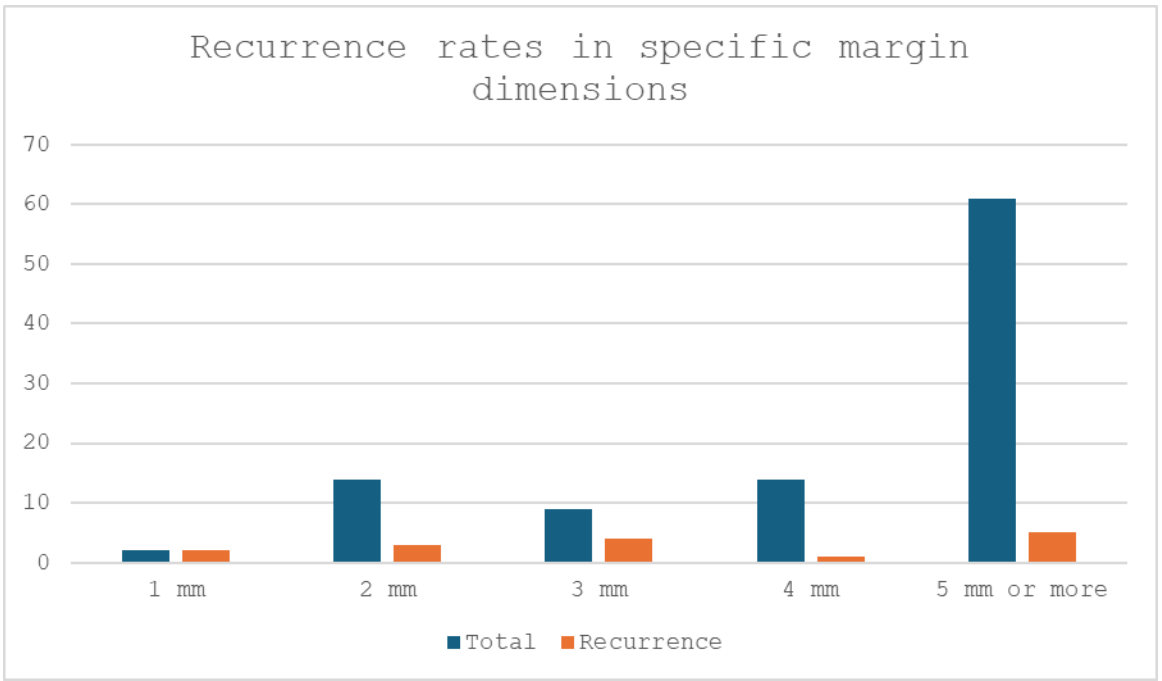

Fig 2

Out of total recurrences (n=15), 13 % was attributed to 1 mm margin, 20 % to 2 mm margin, 26 % to 3 mm margin, 6 % to 4 mm margin, and 33 % of recurrences were seen in 5mm or more. It should be noted that patients who got local recurrence with margin more than 5 mm also had other high risk feature in the final histopathology report. In total, 66.6 % of recurrence was attributed to margins less than 5 mm. It is very clear with these numbers that with each mm decrease in the size of margin the rate of recurrence is increasing.

	Recurrences
1 mm	02
2 mm	03 = 9
3 mm	04
4 mm	01
≥ 5 mm with other risk factors	05
	N = 15

It is worth noting that maximum number of patients who got a recurrence had some or the other adverse high risk features in their final histopathology report accounting for the need of adjuvant therapy.

Among all those with close margins (<5 mm) i.e, n = 39, 60% of local recurrence cases were solely due to margins of ≤ 3mm .

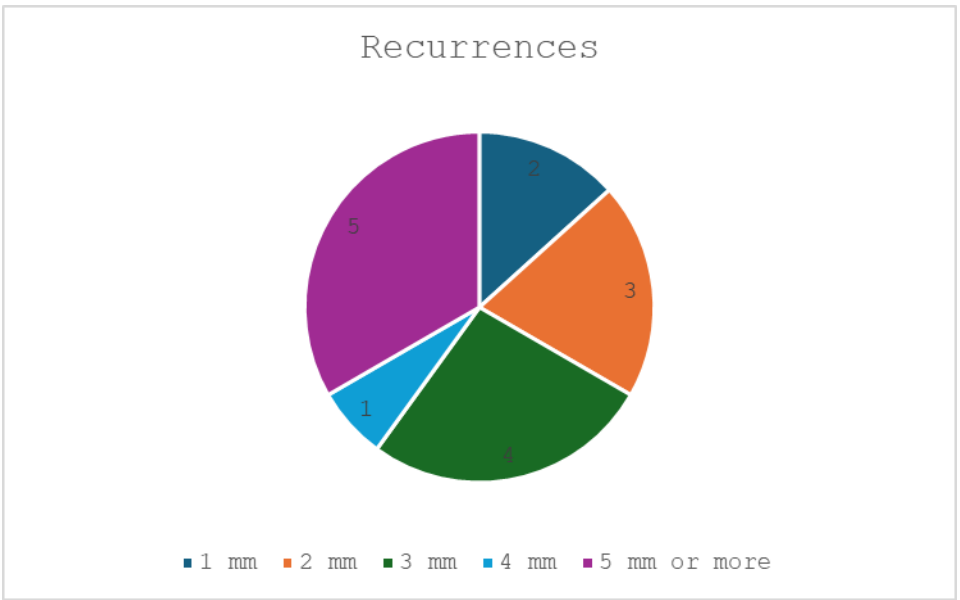

Fig 3

It also came into light that, out of all the 100 patients who were studied, a total of 54 patients had some or the other adverse features. Out of the all patients with adverse features, 13 (24%) patients had local recurrence, among which 9 patients had a delayed onset of adjuvant therapy i.e, more than 6 weeks after the date of surgery and 2 patients had defaulted the adjuvant therapy, and 2 patients had completed the adjuvant treatment on time.

Among total recurrences (n=15), 9 (60%) patients had a history of delayed onset of adjuvant therapy and 2 (13%) patients had defaulted the adjuvant treatment due to various reasons, 1 patient had completeled the adjuvant on time and 3 patients did not require any adjuvant treatment.

Also among all the patients with local recurrences who had an adequate (≥ 5 mm) margin, n = 5, 60 % had occurred in patients with other adverse risk features and history of delayed onset of adjuvant therapy.

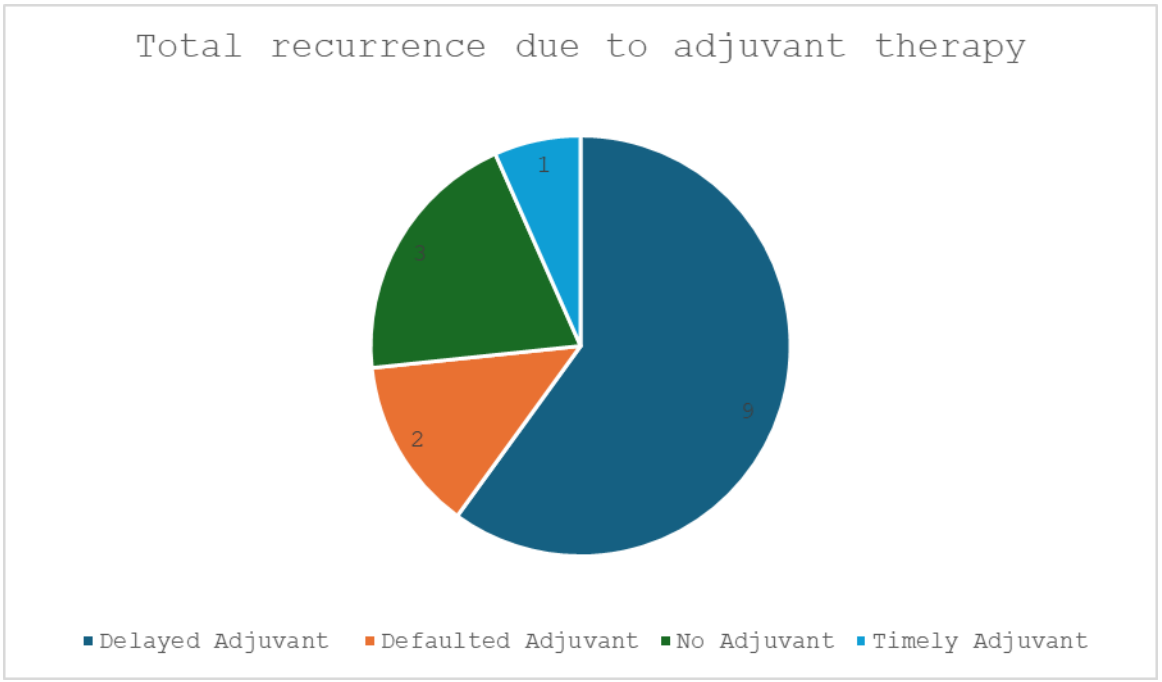

Fig 4

Discussion

In squamous cell carcinoma of the oral cavity, surgical resection with neck dissection is the treatment of choice[15]. The importance of getting negative margins is major for good prognosis of the disease. To achieve this, the most commonly used tool is the frozen section technique. There have been a lot of debate about frozen section efficacy in achieving the adequate negative margin. Although the cost-benefit ratio of the same have been questionable.

It has to be noted that in our analysis, the frozen section technique was not used for negative margins. The period of study is between September 2019 – September 2021, where 100 patients of oral squamous cell carcinoma underwent surgery and were followed up for two years at regular intervals. In this study, the feature of local recurrence was specifically looked for, in a follow up period of two years and was documented.

In our analysis it was found that with every decrease in the size of margin the rate of recurrence was increasing. The maximum rate of recurrence was found in margins less than or equal to 3 mm. The other major factor that was inferred is that even with an adequate margin (≥ 5 mm), there were instances of local recurrence that was directly proportional to the delay in commencement of adjuvant chemo-radiotherapy. According to National comprehensive Cancer Network, the adequate time for starting adjuvant therapy is within 6 weeks of date of surgery[3]. Any delay or breach in this schedule can have unfavourale outcomes in the prognosis of the patient. In this analysis, the factor of local recurrence was only taken into consideration, beacuse the aim of this study was to establish a inversely proportional relationship between the margin status and the local recurrence. The other major factors like disease free survival, overall survival, regional recurrence is beyond the scope of this study.

The fact that frozen section technique is not used in the patients of this study, yet 85 % patients had local recurrence free survival (LRFS) proves that with a skillful surgical resection with wide adequate margins go a long way. This also proves that use of frozen section might not be compulsory required in de-novo cases who have not underwent any kind of treatment of OSCC before. Nevertheless frozen section might be a very useful technique in salvage situations where the morbidity of excessive resection might be more harmful than beneficial.

Another observation of this analysis was that the recurrence rates were also dependent on the time from when the adjuvant treatments were started for patients with close margins and other risk factors in patients with adequate margins. It was found that among total recurrences, 60 % patients had a delayed onset of adjuvant therapy. This can be attributed to the fact that this analysis is been done on patients who were operated between september 2019 – september 2021 that includes the COVID era. The healthcare sytem was severly affected during this time which is a very important factor to prove the delay in the commencement of adjuvant therapy. The same can also be the very reason why 2 patients had defaulted the adjuvant treatment midway and ended up having local recurrence.

Since there have already been numerous studies establishing the importance of margins(3), the cost effectiveness of the same is till questionable. In a public hospital with the patient pool of a economically weaker background the use of financially demanding resources is limited. Hence the scope of finding cost effective solutions is yet to be explored.

The most important thing is to get wide margins intraoperatively and also to focus on quick recovery of the patients post operatively so that the adjuvant therapy is not delayed. The limitation of this study was that only two year follow up data was analysed based on which the results were extracted. In conclusion our study determines the need for more economical ways to examine margins intraoperatively. Also, a larger sample

size with a longer follow up data will give more precise results.

Conclusion

It is very clear with these numbers that with each mm decrease in the size of margin the rate of recurrence is increasing. Even if the margins are adequate, any delay in starting or completing the adjuvant treatment will adversely affect the patient outcome in terms of local recurrence free survival.

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