How to Cite:
ELmoatasem, M., Hamdy, O., Emarah, Z., Elnahas, W., Roshdy, S., & Abdelwahab, K. (2022). Surgical techniques and outcomes in patients with oral cavity cancer after induction chemotherapy. *International Journal of Health Sciences*, *6*(S1), 12607–12622. https://doi.org/10.53730/ijhs.v6nS1.8172

Surgical techniques and outcomes in patients with oral cavity cancer after induction chemotherapy

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***Abstract*---**Objective: Locally advanced Oral squamous cell carcinoma OSCC has a poor prognosis, surgery is mainline for treatment. The role of induction chemotherapy is still controversial. Methodology: This is a prospective study that included 25 patients with locally advanced OSCC who received induction chemotherapy with cisplatin, docetaxel & 5-FU (TPF) protocol regimen followed by surgical intervention. The epidemiological, surgical, and oncological outcomes of all the included patients were analyzed. Results: one patient showed no response, 18 patients had a partial response while 6 patients showed pathological complete response (pCR). Five out of the six patients who achieved pCR did not need reconstructive surgery and also five out of those 6 patients were operated on through a less destructive transoral approach. Consequently, those patients had less operative time, blood loss, hospital stay, and significantly less time to start oral feeding. The median disease-free survival was 15 (12-18) months in patients who attained pCR and 13 (5-24) months in the non pCR group. Conclusion: Pathological complete response after

Manuscript submitted: 18 March 2022, Manuscript revised: 9 April 2022, Accepted for publication: 27 May 2022

induction chemotherapy for locally advanced OSCC is associated with improvement in disease-free survival, less destructive surgery, and less need for flap reconstruction.

***Keywords*---**Oral cancer, squamous cell carcinoma, tongue cancer, pathological complete response, survival.

Introduction

Head and neck squamous cell carcinoma (HNSCC) represents about 90% of all head and neck cancers, and is the sixth most common non-skin cancer in the world, with an incidence of about 600,000 cases per year and a mortality rate approximating 50% (Govindan & DeVita2015). The main risk factors for HNSCC are tobacco use, alcohol consumption, and human papillomavirus (HPV) infection. Despite advances in the knowledge of its epidemiology and pathogenesis, the survival rates for many types of HNSCC showed little improvement over the past four decades. That's why more efforts to understand the pathogenesis of HNSCC are needed to promote the development of improved therapeutic approaches (Stransky et al., 2011).

Within the Middle East, the rates of smoking are high with a limited Alcohol consumption rate; this is especially true for Egypt where smoking rates are increasing for both cigarettes and water-pipe. Previous hospital-based studies from Egypt showed that head and neck cancer (HNC) constitute about 17-20% of all malignancies. A report of the Middle East Cancer Consortium (MECC) of the National Cancer Institute in Bethesda, USA, depicted that Egypt had one of the highest overall incidence rates of cancer of the oral cavity and pharynx (5.5/105) among the Middle East countries (Attar et al., 2010).

The main treatment line for locally advanced oral cavity cancer is surgical resection then chemo-radiotherapy. Neoadjuvant chemo-radiotherapy is considered for tumors that is potentially unresectable (Genden et al., 2010). Studies targeting patients with advanced resectable oral cavity cancer after induction chemotherapy observed a significant preoperative downstaging of the tumor which was translated into less destructive surgery, less need for postoperative radiotherapy but without any improvement in local control or overall survival (Licitra et al., 2003, Bossi et al., 2014).

Zhong et al. (2013) failed to demonstrate that cisplatin, docetaxel & 5-FU (TPF) regimen induction chemotherapy can improve survival if compared to upfront surgery in patients with advanced resectable oral cavity squamous cell carcinoma stage 3 or stage 4a and recommended incorporation of biological agents to the treatment regimen in the future, and identify patients who are more likely to get benefits from induction chemotherapy by using clinical or biomarker criteria. Our study was proposed aiming at the detection of the surgical techniques and options for patients with locally advanced oral cavity squamous cell carcinoma who receive induction chemotherapy and its subsequent effect on the surgical and oncologic outcomes.

Patients and methods

This prospective interventional study was conducted from September 2018 to June 2021 at the surgical oncology unit, Oncology center, Mansoura University (OCMU) including 25 patients with locally advanced oral cavity squamous cell carcinoma. The study was approved by Mansoura Faculty of Medicine-IRB with code number MD.18.09.86. The study included all the patients with pathologically proven oral cavity squamous cell carcinoma (OSCC) who fulfilled the inclusion criteria.

The sample size for this study is determined by an estimation of the magnitude of the anticipated difference in pathological complete response (pCR) that would be detected according to Bossi et al. (2014). Based on the requirement that the difference in pCR in this study will be tested for statistical significance is 28 %, to provide a statistical power level of 0.80 with an α level of 0.05, the minimum sample size is determined to be 25 participants.

Inclusion criteria:

- Patients with confirmed pathology of squamous cell carcinoma (SCC).
- T2–T4/ N0-N2 tumors

Exclusion criteria:

- patients who were unfit for chemotherapy or unfit for anesthesia
- Previously treated patients with any therapeutic modalities

Preoperative evaluation:

- History and complete physical examination
- Demographic information (age, gender) was recorded at the initial visit.
- Relevant medical history including history of oral cavity cancer, smoking, dental problems, other medical comorbidities, and information regarding underlying diseases was recorded
- A complete physical examination was performed by qualified staff.
- Body temperature, blood pressure, pulse, and respirations were assessed before each cycle of chemotherapy after resting for 5 minutes
- The needed laboratory investigation either before the initiation of chemotherapy or before general anesthesia was performed

Radiological investigations:

- Post-contrast head and neck MRI to delineate the primary tumor
- Neck Ultrasonography to assess the cervical nodal status
- Chest non-contrast CT to exclude lung metastasis.

Pathological diagnosis:
Wedge biopsy from the ulcer to confirm diagnosis and grade.

Written consent:
A written consent with a simplified explanation of the lines of management and the possible complications were signed by the patient before starting treatment.

Chemotherapy;
The Patients received three cycles of cisplatin (75 mg/m2), docetaxel (75 mg/m2), and fluorouracil (750 mg/m2), as a 120-h infusion administered every three weeks. Those who did not show any response after the second cycle were referred for chemo-radiotherapy or surgery. Any toxicity from chemotherapy was recorded and the dose was adjusted to overcome such toxicities. Reevaluation with clinical examination, head and neck postcontrast MRI, and neck Ultrasonography was done after the end of induction chemotherapy by two weeks at least.

Surgery
Surgery was performed after 2 weeks at least after completion of induction chemotherapy. General anesthesia with trans-nasal endotracheal intubation and nasogastric feeding tube insertion from the other nostril and urinary catheterization. Excision of the primary lesion was done trans-orally or with lip splitting or through compartmental resection. The excision was performed with 1 cm gross safety margins all around and confirming negative margins with frozen sections.

The type & complexity of surgery were determined according to the tumor site and extension either wide local excision (WLE) with primary closure or reconstruction with a submental flap, supraclavicular artery island flap, a buccal pad of fat, and tongue flap. Block neck dissection for all patients was done for ipsilateral cervical lymph nodes.

Postoperatively the patients received nasogastric tube feeding from the first postoperative day. The patients were followed up within the inpatient ward and ICU admission was needed in selected patients for close monitoring of the airway for fear of any obstruction by postoperative edema. The patients were referred to medical oncology postoperatively for adjuvant treatment with radiotherapy if close or positive margins, presence of perineural or vascular invasion, pathological T3-4 or N2-3, or extranodal tumor extension. Follow up with clinical examination, post-contrast MRI every 3 months after clinical assessment for the first year to detect any local or nodal recurrence.

Statistical analysis and data interpretation:
Data were fed to the computer and analyzed using IBM SPSS Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Qualitative data were described using numbers and percentages. Quantitative data were described using median (minimum and maximum) for non-parametric data and mean, the standard deviation for parametric data after testing normality using Kolmogorov-Smirnov test. The significance of the obtained results was judged at the (0.05) level.

Data analysis
Qualitative data:
- Chi-Square test for comparison of 2 or more groups
- Fischer Exact test was used as a correction for the Chi-Square test when more than 25% of cells have a count less than 5 in 2*2 tables.
- Monte Carlo test as correction for Chi-Square test when more than 25% of cells have count less than 5 in tables (>2*2).

Quantitative data:
Parametric tests:
Student t-test was used to compare 2 independent groups

Non Parametric tests:
Mann-Whitney U test was used to compare 2 independent groups

Kaplan-Meier test
Used to calculate overall survival and disease-free survival with using log-rank x^2 to detect the effect of risk factors affecting survival.

Cox regression:
Used to calculate predictors affecting overall survival and disease-free survival with the calculation of hazard ratio.

Results

Epidemiological, patient-related, and tumor-related data:
This is a prospective study that included 25 patients with locally advanced oral cavity squamous cell carcinoma.
The study included 11 male patients (44%) and 14 females (56%). The mean age at presentation was (53.52±11.8years) ranging from (28-69 years). **Table (1)** shows basic epidemiological and clinical data.

Table (1)
Demographic & medical characteristics of the studied patients

		n=25	%
Age/years		53.52±11.8 (28-69)	
Sex			
Male		11	44.0
Female		14	56.0
Smoking			
no		16	64.0
yes		9	36.0
Dental problems			
no		12	48.0
yes		13	52.0
HBV		0	0.0
HCV		8	32.0
Co-morbidities	Hypertension	5	20
	DM	3	12
	Chronic liver disease	1	4
	IBD	1	4

Regarding the primary tumor site among the studied patients;16 patients had tongue squamous cell carcinoma (60%), 6 patients had buccal mucosal carcinoma

(24%) and 4 patients had carcinoma in the retromolar trigone (16%). The main tumor size before chemotherapy was 4.14±0.85 cm which was decreased to 2.02±0.68 cm after chemotherapy. 8 tumors were Grade 1 (32%), 13 tumors were Grade 2 (52%) and 4 tumors were Grade 3 (16%). Seven patients (28%) had node-negative N0 disease, 4 patients (16%) had N1 disease, one patient (4%) had N2a disease, 11 patients (44%) had N2b disease and 2 patients had N2c disease. (Table 2)

Table 2
Tumor characters of the included patients

	n=25	**%**
Primary site		
Tongue	15	60.0
Retromolar	4	16.0
Buccal	6	24.0
Grade		
1	***8***	***32.0***
2	***13***	***52.0***
3	***4***	***16.0***
Nodal status before chemotherapy		
N0	**7**	**28.0**
N1	**4**	**16.0**
N2A	**1**	**4.0**
N2B	**11**	**44.0**
N2C	**2**	**8.0**

Chemotherapy related complications:
The recorded complications related to induction chemotherapy agents were; 20 patients presented with stomatitis, 13 patients with alopecia (52%), 14 patients (56%) with Non-Neutropenic fever (NNF), 8 patients (32%) with diarrhea, 5 patients (20%) with neuropathy and 4 patients (16%) with elevated liver enzymes.
Operative and postoperative statistics (Table 3):

Table (3)
Operative and postoperative data

	n=25	%
Technique:		
Transoral	12	48.0
Lip splitting	9	36.0
Compartmental resection	4	16.0
Mandibulectomy:		
No	21	84.0
Marginal	4	16.0
Lymph node dissection level		
1-4	12	48.0
1-5	11	44.0
Bilateral (1-5)	2	8.0

Reconstruction		
No	9	36.0
Cervicofacial flap	2	8.0
Buccal pad of fat	5	20.0
Submental flap	4	16.0
Supraclavicular flap	3	12.0
Tongue flap	1	4.0
Thiersch graft	1	4.0
Postoperative complications:		
Pulmonary embolism	1	4
Salivary leakage		
no	21	84
yes	4	16
Infection	n=18	
minimal	2	11.1
mild	12	66.7
moderate	3	16.7
severe	1	5.6
wound gap		
no	18	72
yes	7	28
Flap loss	n=15	
No	12	80.0
Partial loss	2	13.3
Full loss	1	6.7
revision surgery	4	16
Secondary sutures	2	50
Flap refashioning	2	50

The approach for tumor resection was variable according to tumor site and size; the transoral approach was used in 12 patients (48%) (Figure 1-a), lip splitting incision in 9 patients (36%) (Figure 1-b), and compartmental tongue resection in 4 patients (16%). In 4 patients only, marginal mandibulectomy was required.

Nine patients (36%) did not require any reconstructive methods after tumor resection (Figure 2-a), while in sixteen patients, a reconstructive tool was used. Five patients (20%) underwent reconstruction with a buccal pad of fat (Figure 2-b), two patients (8%) underwent reconstruction with cervicofacial flap, four patients (16%) with submental flap, three patients (12%) with supraclavicular island flap (Figure 2-c), one patient (4%) with tongue flap and another one (4%) with Thiersch graft.

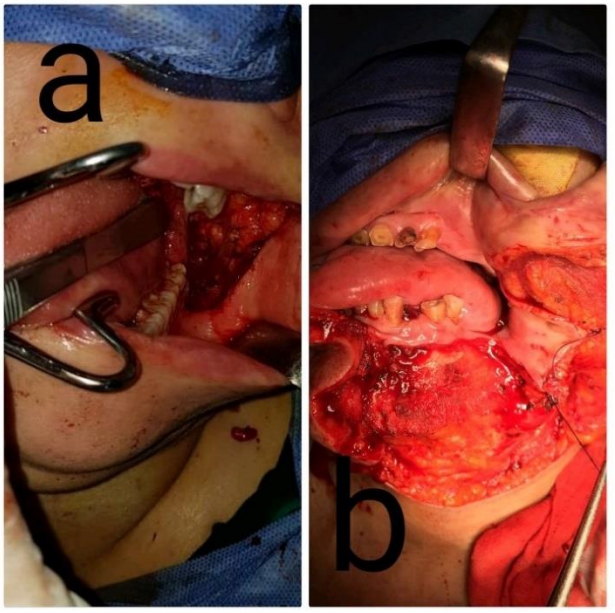

Figure 1: approaches for resection of 1ry tumor (a)transoral approach, (b)lip splitting approach

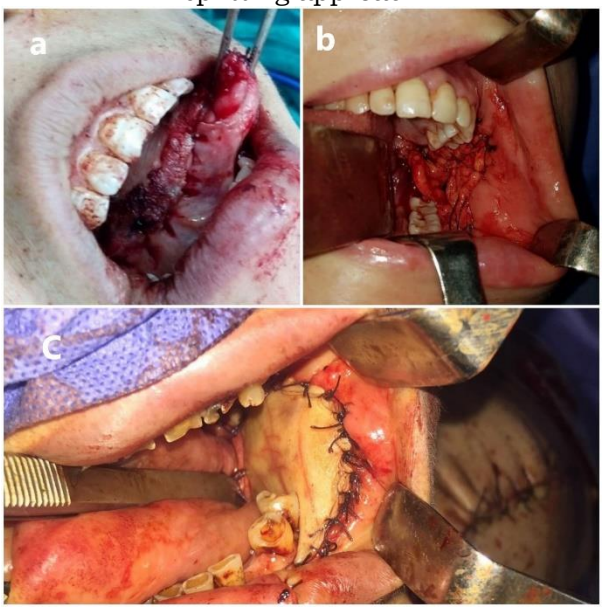

Figure 2: Different methods for reconstruction: (a) primary closure, (b) buccal pad of fat (c) supraclavicular artery island flap.

The mean operative time was 223.0±81.15 minutes, the mean blood loss intraoperative was 308±91.10 ml, the median number of hospital stay length was 7.0 (2.0-23.0) days and the median number of days before starting oral feeding was 5.5 (3.0-23.0) days.

The recorded postoperative complications among the studied patients were:

- Salivary leakage in 4 patients (16%)
- Infection:
  - Minimal to mild in 14 patients in whom infection was managed conservatively
  - Moderate to severe in 4 patients.
- Wound gap was recorded in seven patients (28%), two of them were managed with secondary sutures.

Only one patient died in the early postoperative period because of massive pulmonary embolism.

Pathological outcome and pathological complete response:

Regarding the response of the primary tumor site to induction chemotherapy, only one patient showed no response **(Figure 3)**, 18 patients had a partial response **(Figure 4)** while 6 patients showed pathological complete response (PCR) **(Figure 5)**. The median number of excised lymph nodes was 17 (7-36). The median number of infiltrated LNs was 1.0 (0-10).

Figure 3: no clinical response to induction chemotherapy: (a) before, (b) after 3 cycles.

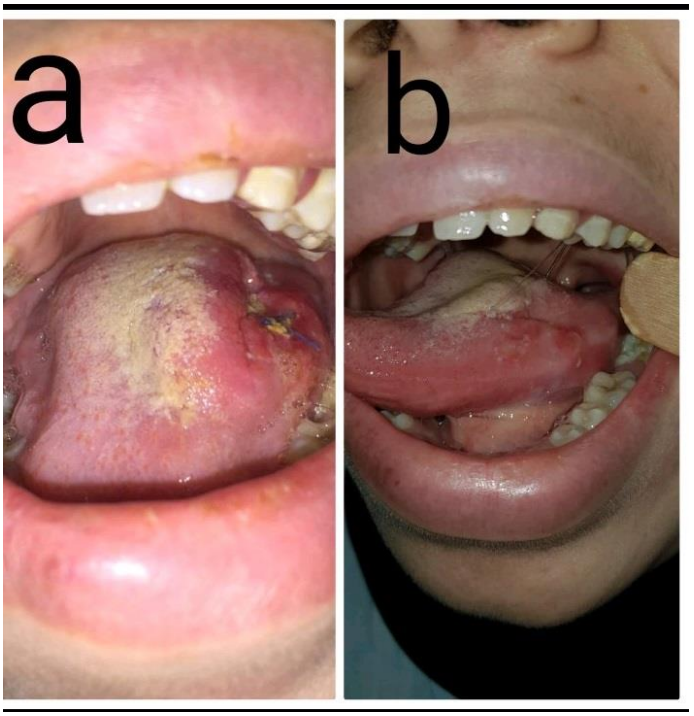

Figure 4: complete clinical response to induction chemotherapy: (a) before, (b) after two cycles, (c) after 3 cycles.

Figure 5: partial clinical response to induction chemotherapy: (a) before, (b) after 3 cycles

None of the demographic characteristics, medical characters, and tumor characters showed a significant relation with the rates of PCR. Only lymph node status showed a significant relation with PCR (Table 4).

In five of the six patients in whom PCR was achieved, reconstructive surgery was not needed and only one case (16.7) required reconstruction with a buccal pad of fat but there is still no statistically significant relationship between the type of reconstruction and pathological response. In addition, also five of them (83 %) had the tumor resected through a transoral approach only while marginal mandibulectomy was needed only in one patient. Consequently, those patients had less operative time, blood loss, hospital stay, and significantly less time to start oral feeding (Table 5). During follow-up, tumor recurrence occurred only in one patient with PCR while among the other group who didn't achieve PCR 9 patients developed either local or nodal recurrence (6 patients at the primary tumor site and three patients developed nodal recurrence) (Figure 6).

Discussion

Oral squamous cell carcinoma (OSCC) occurs predominantly in middle-aged and older individuals with prolonged tobacco or alcohol consumption (Beynon et al., 2018)**.** However, other studies have reported that the incidence in young adults was increased (Shiboski et al., 2005, Patel et al., 2001). Tobacco or alcohol use may not be the etiology of OSCC in young adults, Gong et al. (2019) study has demonstrated that only 7% (11/156) patients were heavy smokers [11]. Our results were similar to previous results; we have only 9 out of 25 patients (36%) who were smokers but we detected other factors as chronic irritation by sharp dental problems in 13 cases (52%).

The incidence of OSCC shows male predominance, with a male-to-female ratio of about 2: 1 (Licitra et al., 2003, Zhong et al. (2013). However, the incidence of OSCC has been increasing in young white women, with a male-to-female ratio of 1.6: 1 (Patel et al., 2001). In our study, we observed a predominance of female cases 14 to 11 males with ratio male-to-female ratio of 1:1.27.

Neoadjuvant (induction) chemotherapy (IC) means administration of chemotherapy before definitive therapy which either may be surgery or RT or RT+CT. Its role in head and neck SCC is being studied questioning its effect on the surgical intervention plan with organ preservation by tumor down-staging, decreasing locoregional relapse, and decreasing the rates of distant spread. Yet, the indications of neoadjuvant therapy in oral cavity SCC are still not clearly defined **[**Licitra et al., 2003, Bossi et al., 2014, Zhong et al., 2013, Ma et al., 2013).

The first randomized phase III study using triple therapy TPF induction followed by surgery compared with up-front surgery in patients with resectable OSCC was done by Zhong et al. (2013) the study concluded that induction chemotherapy with TPF was not associated with unexpected complications and did not increase perioperative morbidity. the most frequent recorded side effects by Zhong et al. (2013) were alopecia (70.5%), nausea and/or vomiting (55.7%), hematologic

toxicity (28.7%), altered liver function tests (19.7%), diarrhea (14.8%). Our study results showed similar expected side effects of the induction chemotherapy as 20 patients (80%) developed stomatitis, 13 patients with alopecia (52%),14 patients (56%) with Non Neutropenic fever NNF, 8 patients (32%) with diarrhea, 5 patients (20%) with neuropathy (Zhong et al., 2013).

Table (4)
Association between socio-demographic characteristics, medical characters, tumor characters, and pathological response among studied cases

	no or Partial response (n=19	PCR (n=6)	test of significance
Age/years mean±SD	54.0±12.10	52.0±7.67	t=0.378 p=0.709
Sex Male Female	N(%) 8(42.1%) 11(57.9%)	N(%) 3(50.0%) 3(50.0%)	 FET P=1.0
Smoking -ve +ve	 13(68.4) 6(31.6)	 3(50.0) 3(50.0)	 FET P=0.630
BMI(Kg/m^2) mean±SD	33.50±5.6	32.18±7.86	t=0.457, p=0.652
Dental problems -ve +ve	 8(42.1) 11(57.9)	 4(66.7) 2(33.3)	 FET P=0.378
Tumor size (longest diameter) before treatment	4.23±0.89	3.87±0.65	t=0.905 p=0.375
Grade 1 2 3	 4(21.1) 11(57.9) 4(21.1)	 4(66.7) 2(33.3) 0(0.0)	 MC P=0.093
Nodal staging N0 N1 N2A N2B NC	 5(26.3) 4(21.1) 0 9(47.4) 1(5.3)	 2(33.3) 0 1(16.7) 2(33.3) 1(16.7)	 MC p=0.244
Positive nodal status by radiology before treatment	18(94.7%)	1(16.7%)	FET , P=0.0001*
HCV	7(36.8%)	1(16.7%)	x^2=0.853 P=0.356
Associated co-morbidities	8(42.1)	2(33.3)	FET P=1.0
Primary site Tongue Retromolar Buccal	 10(52.6) 3(15.8) 6(31.6)	 5(83.3) 1(16.7) 0	 MC P=0.271

x^2=Chi-Square test, MC: Monte Carlo test, FET: Fischer exact test *statistically significant if p<0.05

Table (5)
Association between pathological response and operation characteristics among studied cases

Technique	no or Partial response (n=19)	PCR (n=6)	test of significance
Bleeding/mm	330(140-450)	210(170-390)	Z=1.85 P=0.064
Operative duration/ minutes	240(120-420)	150(120-300)	Z=1.76 P=0.07
Hospital stay/days	7(3-23)	5(2-7)	Z=2.37 P=0.02*
Days of starting oral intake	7.0(3.0-23.0)	5.0(4.0-5.0)	Z=2.10 P=0.035*

Z: Mann Whitney U test *statistically significant if p<0.05

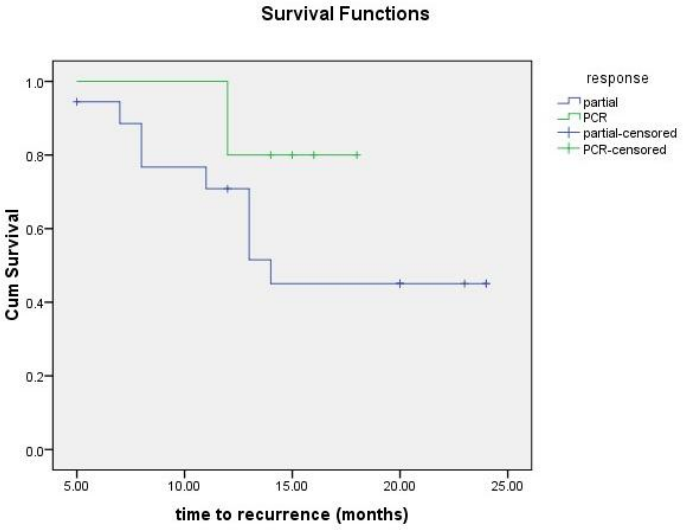

Figure 6: Kaplan Meier curve for the effect of pathological response on disease-free survival (partial or complete response)

Also, Zhong et al. (2013) concluded that Patients who received TPF induction with favorable pathologic or clinical response had a decreased risk for death and recurrence. In our short term study of using induction chemotherapy regimen TPF, our results were coping with Zhong et al. (2013) we detected a tumor recurrence in one of six cases who developed PCR, while it was much higher between the cases who didn't achieve PCR after induction chemotherapy; 9 of 18 cases developed locoregional recurrence after a median follow up 14 months (5-24).

Patil et al. (2013) compared IC with TPF or TP and assessed for resectability. The response rate with the TPF and TP regimens was 32% and 27.37%, respectively. Surgical resection could be performed in 68% and 37.89% respectively. The estimated median OS was 12.7 months, for the whole cohort which was significantly better than those who received non-surgical management after chemotherapy. Those results demonstrated the ability of IC to fascilitate radical surgery with comparable 2 years survival to primary radical surgery (Patil et al., 2013). Similar results were confirmed by the same research group in a larger follow-up study (Patil et al., 2014).

PCR occurred in 16 patients (13.4%) of the patients who received induction chemotherapy with Zhong et al. (2013) but it was much higher in our study 24% (6 patients), Licitra et al. (2003) reported pathologic complete response of the primary tumor in 22 patients (27%), in this study most of the nodal stage was N0 in 57.1% of patients, 26.5% with N1and 16.4% with N2((Licitra et al., 2003, Zhong et al. (2013).

Despite the lower N stage recorded by Licitra et al. (2003) in comparison to the N stage in our study but the PCR ratio was nearly equal 27% vs. 24% respectively. This could be explained by the better effect of triple therapy regimen TPF in our study compared to double therapy regimen PF in Licitra et al. (2003) study, further analysis of the nodal status of the cases who developed PCR in other studies is needed.

A retrospective and observational study done by Patel.et al. (2021) including 67 patients enrolled in this study, 35 patients underwent upfront radical surgery (non-NACT group) and 32 patients received NACT followed by surgery (NACT group). All patients (100%) of 32 patients included in the neoadjuvant chemotherapy group had radical surgery with flap reconstruction**.** In our study we recorded that 9 patients (36%) did not require any reconstructive methods after tumor resection, 5 patients (20%) underwent reconstruction with a buccal pad of fat,2 patients (8%) were reconstructed with cervicofacial flap, 4 patients (16%) with submental flap, 3 patients (12%) used supraclavicular island flap, one patient (4%) with tongue flap and one patient (4%) with Tiersch graft after hemiglossectomy. So, we can say that IC may offer a more conservative organ preserving surgery by deintensification of the loco-regional surgical technique provided that we can attain a good safety margin with 1 cm at least.

After 11.5 years of Long-term follow-up randomized trial, Bossi et al. (2014) suggested that no difference in OS and DFS, loco-regional and distant metastasis relapse at 10 yrs. But in patients with PCR had a significant survival improvement when compared with those who did not achieve PCR (10-year OS: 76.2% versus 41.3%, P. = 0.0004; HR 0.230). Bossi et al. (2014) correlated the survival benefit to the improvement in loco-regional control of the disease; the loco-regional recurrence in patients achieving PCR was 11.1% while it was 32.7% in patients with residual tumor after induction chemotherapy with P. value = 0.0289 (Bossi et al., 2014).
Our study results were in line with the observation made in Bossi et al. (2014) study; locoregional tumor recurrence occurred in only one of 6 patients with PCR (16.7%) during follow up while among the other group who didn`t achieve PCR

was in 9 patients (50%) with p. value *(P.=0.339)*, The median disease-free survival was 15 (12-18) months in patients who attained PCR and 13(5-24) months in the non-PCR group but P. value between the two groups was not significant *(P.=0.708)*. In Bossi et al. et al. (2014) study 22 of 82 operated patients showed PCR nine cases in mouth floor, six tongue cases, 4 cases in retromolar trigone, the alveolar margin in two cases, and buccal mucosa in one case, but in our study between 6 patients had PCR: 5 of them had tongue cancer and only one patient with SCC in the retromolar trigone. This difference could be explained by our small group of patients.

Licitra et al. (2003) reported a significant decrease in the rate of mandibulectomy with tumor resection with induction chemotherapy was performed in 52% of patients but only in 31% in the induction chemotherapy arm. Our study recorded 4 cases (16%) who required marginal mandibulectomy, Three of them didn't have PCR and one case had PCR. The rate of mandibulectomy was much lower with our study because of the primary site of included cases, in Licitra et al. (2003) about 42% of included cases in the induction chemotherapy arm were in mouth floor and gingival margin which explains the rate of mandibulectomy 31%, but in our study, most of the included patients were in tongue 60% which usually does not need mandibulectomy during resection.

Conclusion

Pathological complete response after induction chemotherapy for patients with locally advanced oral cavity cancer is associated with an improvement in disease-free survival, less destructive surgery, and less need for flap reconstruction. Further studies are needed to identify other predictors for a pathological complete response to achieve better patient selection criteria and offer better surgical and oncological outcomes.

References

Attar, E., Dey, S., Hablas, A., Seifeldin, I. A., Ramadan, M., Rozek, L. S., & Soliman, A. S. (2010). Head and neck cancer in a developing country: a population-based perspective across 8 years. Oral oncol. 46(8), 591-596.

Beynon, R. A., Lang, S., Schimansky, S., Penfold, C. M., Waylen, A., Thomas & Ness, A. R. (2018). Tobacco smoking and alcohol drinking at diagnosis of head and neck cancer and all-cause mortality: Results from head and neck 5000, a prospective observational cohort of people with head and neck cancer. Int J Cancer, 143(5), 1114-1127.

Bossi, P., Vullo, S. L., Guzzo, M., Mariani, L., Granata, R., Orlandi, E. & Licitra, L. (2014). Preoperative chemotherapy in advanced resectable OCSCC: long-term results of a randomized phase III trial. Ann Oncol. 25(2), 462-466.

Genden, E. M., Ferlito, A., Silver, C. E., Takes, R. P., Suárez, C., Owen, R. P. & Rinaldo, A. (2010). Contemporary management of cancer of the oral cavity. Eur Arch Oto-Rhino-Laryngol. 267(7), 1001-1017.

Gong, Y., Ju, H., Ren, G., & Wu, Y. (2019). Cisplatin based induction chemotherapy modified by ERCC1 improved the outcome of young adults with locally advanced oral squamous cell carcinoma. J Cancer, 10(9), 2083.

Govindan, R., & DeVita, V. (2015). DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology Review.

Licitra, L., Grandi, C., Guzzo, M., Mariani, L., Vullo, S. L., Valvo, F. & Cantu, G. (2003). Primary chemotherapy in resectable oral cavity squamous cell cancer: a randomized controlled trial. J Clin Oncol. 21(2), 327-333.

Ma, J., Liu, Y., Yang, X., Zhang, C. P., Zhang, Z. Y., & Zhong, L. P. (2013). Induction chemotherapy in patients with resectable head and neck squamous cell carcinoma: a meta-analysis. World J Surg Oncol. 11(1), 1-7.

Patel, D., Saldanha, E., Joseph, B., Dhakad, V., & Desai, S. (2021). Role of Neoadjuvant Chemotherapy in Oral Cavity SCC: A Surgical Oncologists Experience at Tertiary Care Institute. Eur J Clin Oncol. 3(1), 1-4.

Patel, S. C., Carpenter, W. R., Tyree, S., Couch, M. E., Weissler, M., Hackman, Chera, B. S. (2011). Increasing incidence of oral tongue squamous cell carcinoma in young white women, age 18 to 44 years. J Clin Oncol. 29(11), 1488-1494.

Patil, V. M., Noronha, V., Muddu, V. K., Gulia, S., Bhosale, B., Arya, S. & Prabhash, K. (2013). Induction chemotherapy in technically unresectable locally advanced oral cavity cancers: does it make a difference?. Indian J cancer, 50(1), 1.

Patil, V. M., Prabhash, K., Noronha, V., Joshi, A., Muddu, V., Dhumal, S. & Dcruz, A. (2014). Neoadjuvant chemotherapy followed by surgery in very locally advanced technically unresectable oral cavity cancers. Oral Oncol. 50(10), 1000-1004.

Shiboski, C. H., Schmidt, B. L., & Jordan, R. C. (2005). Tongue and tonsil carcinoma: increasing trends in the US population ages 20–44 years. Cancer, 103(9), 1843-1849.

Stransky, N., Egloff, A. M., Tward, A. D., Kostic, A. D., Cibulskis, K., Sivachenko, A. & Grandis, J. R. (2011). The mutational landscape of head and neck squamous cell carcinoma. Sci. 333(6046), 1157-1160.

Zhong, L. P., Zhang, C. P., Ren, G. X., Guo, W., William Jr, W. N., Sun, J. & Zhang, Z. Y. (2013). Randomized phase III trial of induction chemotherapy with docetaxel, cisplatin, and fluorouracil followed by surgery versus up-front surgery in locally advanced resectable oral squamous cell carcinoma. J Clin Oncol. 31(6), 744.