# Predictors of Complications After Flap Reconstruction of Oral Cavity Defects Following Ablation of Squamous Cell Carcinoma

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## ABSTRACT

**Background:** Head and neck cancers represent the sixth most common cancer worldwide with an incidence of over 600,000 new cases per year. More than 90% of head and neck cancers are squamous cell carcinomas (SCC) that arise from the mucosal surfaces of the oral cavity, oropharynx and larynx.

**Objective:** The aim of the current work was to investigate the predictors of complications after flap reconstruction of oral cavity defects following ablation of squamous cell carcinoma.

**Patients and methods:** This prospective comparative study included a total of 41 patients who diagnosed to have oral SCCs, attending at the outpatient clinic of Head and Neck Surgery Unit, National Cancer Institute (NCI), Cairo University and Aswan University Hospital. Written informed consent of all the subjects was obtained after explaining the benefits and hazards for each method step. This study was conducted between 2015 to 2018. Approval of the ethical committee was obtained.

**Results:** Patients with positive history of neoadjuvant chemoradiotherapy (CRTH) are 52% less likely to developing complications than those with negative history of neoadjuvant CRTH. Detection of the short-term oncologic outcome; in the 4 flaps was better in contralateral submental island flap (CSMIF) cases than others. CSMIF were found to be 58% less liable for recurrence in comparison with pectoralis major myocutaneous flap (PMMCF) that was why it didn't show any clinical or radiologically detectable recurrence within the period of 24 months postoperatively. Thoracodorsal artery perforator (TDAP) flaps were 2.6 times more liable for recurrence in comparison with PMMCF. RFFF flaps were found to be 1.2 times more liable for recurrence in comparison with PMMCF.

**Conclusion:** The chosen 4 flaps for this study are applicable to be used for post ablative oral cavity reconstruction. Our flaps were equal in suitability for defect coverage (50-60%).

**Keywords:** Flap reconstruction, Oral cavity, Squamous cell carcinoma, PMMCF, CSMIF, RFFF, TDAP.

## INTRODUCTION

Surgical intervention for head and neck tumors may cause significant soft tissue, bony and skin defects. This may produce functional impairment such as swallowing and speech deficits. Thus, the principle objective of reconstructive surgery after oral cancer ablation is maintaining the functional integrity of the different areas in the oral cavity with restoration of acceptable cosmesis (aesthetic look) using local and loco-regional flaps or even free flaps [(1)].

Reconstruction should be tailored to the patient's ability to cope with a long operation and the risk of substantial morbidity. The reconstructive ladder starting from skin grafts and ending with free flaps may not always be able to be followed due to anatomical and functional requirements of the defects [(2, 3)].

A large number of regional flaps have been proposed for soft tissue reconstruction of the oral cavity with varying success. Local flaps such as nasolabial flaps provide thin reliable skin tissue suitable for repairing, only again, in small defects. The pedicled flaps commonly used for oral reconstruction include pectoralis major myocutaneous flap, forehead flap and platysma myocutaneous flaps [(2)] and skin flaps like submental artery flap and buccal pad of fat flaps [(4)].

In 1979, the Pectoralis Major Myocutaneous flap (PMMCF) was well introduced by Ariyan as one of the significant reconstructive options because of its simple technical aspects (PMMCF in either its myocutaneous or myofascial forms has been a workhorse flap for intraoral reconstruction) and versatility [(5)].

In 1993, The Submental artery island flap (SMIF) was first introduced by Martin and was widely accepted by reconstructive surgeons working in the field of maxillofacial or head and neck reconstruction [(6)].

The radial forearm free flap (RFFF) is very useful flap for soft tissue intra-oral reconstruction. The vascular territory is reliable and offers significant versatility as either a fasciocutaneous, fascial, or osteocutaneous flap [(7)].

In 1995, Angrigiani et al. were the first to describe the thoracodorsal artery perforator flap



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(TDAP) in reconstructive surgery (breast, thorax, limbs), which is also suitable for the repair of head and neck defects [8].

The aim of the current work was to investigate the predictors of complications after flap reconstruction of oral cavity defects following ablation of squamous cell carcinoma.

## PATIENTS AND METHODS

This prospective comparative study included a total of 41 patients who diagnosed to have oral SCCs, attending at the outpatient clinic of Head and Neck Surgery Unit, National Cancer Institute (NCI), Cairo University and Aswan University Hospital. Written informed consent of all the subjects was obtained after explaining the benefits and hazards for each method step. This study was conducted between 2015 to 2018.

**Ethical approval:**
**Approval of the ethical committee of Aswan University was obtained.**

**Inclusion criteria:**
Any patient diagnosed to have oral cavity cancer of SCC type.

**Exclusion Criteria:**
- Patients who had Non- SCC types of oral cavity cancer.
- Patients who had advanced disease; metastatic lesions away from the head and neck region.
- Patients who had another primary lesion away from the head and neck region.
- Patients who were medically unfit for surgery, major cardio-pulmonary diseases…etc.

The included subjects were divided into four groups; **Groups 1 and 2** consisted of 20 cases who were reconstructed by pedicled flaps. **Groups 1 (G1)** included 10 cases who were reconstructed with PMMCF (Pectoralis Major Myo-Cutaneous Flap) and **Groups 2 (G2)** included 10 cases who were reconstructed with CSMIF (Contralateral Submental Island Flap). **Group 3 and 4** consisted of 21 cases who were reconstructed with micro-vascular free flaps. **Groups 3 (G3)** included 11 cases who were reconstructed with RFFF (Radial Forearm Free Flap) and **Groups 4 (G4)** included 10 cases who were reconstructed with TDAP (Thoracodorsal Artery Perforator Flap).

All selected patients were subjected to the following; full history taking and thorough clinical examination, certain preoperative clinical tests, investigations and postoperative care and follow-up strategies for a period of 12-24 months.

**Intraoperative (Surgical Technique):**

- Operations were performed under general anesthesia by NCI Head and Neck Surgery Unit team and Aswan University Hospital team.
- Patient position; mostly in supine position ( except when TDAP flap was harvested, the patient was put in right or left lateral decubitus position according to site from which the flap will be take.
- Urinary catheterization was done to evaluate the fluid output during the operation and postoperatively.
- Scrubbing by povidine-iodine and brushing superiorly from scalp hairline , curving with hairline to post-auricular region till nape and downwards involving face , neck and reach to upper chest (for SMIF or RFA flaps), umbilicus (for PMMCF), chest , umbilicus and flank (for TDAP flap) with scrubbing of forearm and hand (for RFFF).

**Postoperative assessment and Follow-up strategies; this ranged between 12-24 months:**
***This period was for:**
- Assessment of tumor ablation status with early detection of recurrence.
- Assessment of the chosen reconstructive flap; flap related complications.

***This period was divided into early** and **late** follow-up periods:

**Early follow-up**; (for the 1st 4 weeks postoperatively)
- Postoperatively patients were kept in appropriate positions, avoid over-extension of the neck to minimize the tensile strength, pressure points or torsion on the pedicle (for pedicled flaps).
- During this early follow-up period we followed;
- General condition of the patient.
- Operative time.
- Flap viability.
- Donor and recipient sites morbidity; bleeding, infection, healing process.
- Head and neck complications; nerves injury during ND, facial nerve injury, fistulae (orocutaneous salivary fistulae, chylous fistula … etc).

**Late follow-up**; (from the beginning of 2nd month to the end of the 24th month postoperatively), during this late follow-up period we followed;
- Tumor ablation and early detection of locoregional recurrence.

- For assessment (follow up) of tumor ablation and early detection of recurrence:

- As long as about 70% of recurrences occur in the first year, we planned for six postoperative times for follow up scheduled as following; after 1 month , after 3 months, after 6 months, after 12 months, after 18 months and finally at end of 24 months.
- At each of these six times, the patient was assessed by;
  - History taking (especially asking about any new complaints).
  - Clinical examination (especially head and neck region).
  - Radiological (U/S +/- CT or MRI) examination.

***Statistical analysis***

**Sample size:** The statistical power of the study was calculated using the results from OpenEpi, version 3, open source calculator SS proper to determine an adequate sample size for this study. With accuracy mode calculation and an effect size convention 7.9 for the independent samples t-test, with probability of 0.05, provided 80% power for sample size of 20 patients in each group.

- All demographic characters, operative details, intraoperative and postoperative complications all were recorded.
- All gathered data were verified, coded by the researcher and statistically analyzed using IBM-SPSS 21.0 **(IBM-SPSS. Statistical Package for Social Science. Ver. 21. Standard deviation. Copyright© SPSS Inc., 2011-2012. NY, USA.2012).**
- Descriptive statistics; Means and standard deviations were calculated.

- Tests of significance;
  - **Chi-square test;** was used to compare the difference in distribution of frequencies among different groups.
  - For continuous variables with more than two categories, **ANOVA test** was calculated to test the mean differences of the data that follow normal distribution.
  - Independent sample **Kruskal-Wallis** was used to compare the median difference between groups that don't follow normal distribution.
  - **Post-hoc test** was calculated using Bonferroni corrections.
- A probability value (p-value) is considered to be statistically significant if it is $\leq$ 0.05.

**RESULTS**

On starting work preparation for this study, we collected data of 58 patients but unfortunately 17 patients were not included (as 2 patients died on the first postoperative week, 10 patients died during the first 12 months postoperatively, 3 patients travelled abroad and were not be able to be involved in our study and 2 patients we failed to have a continuous contact with them as they preferred to continue their postoperative follow up in medical centers near their places of residency) and so only 41 patients were included and successfully completed the 24 months needed for the short term period of postoperative follow up designed according to the strategy of this study. The results of the follow up of those 41 patients were discussed as mentioned below.

10 (24.4%) patients had PMMCF reconstruction and called group 1, G1 (PMMCF) patients, 10 (24.4%) patients had CSMIF reconstruction and called group 2, G2 (CSMIF) patients, 11 (26.8%) patients had RFFF reconstruction and called group 3, G3 (RFFF) patients and 10 (24.4%) patients had TDAP reconstruction and called group 4, G4 (TDAP) patients.

In G1 (PMMCF), the youngest patient had a 37 years old and the oldest had a 66 years old, in G2 (CSMIF), the youngest patient had a 50 years old and the oldest had a 78 years old, in G3 (RFFF), the youngest patient had a 27 years old and the oldest had a 68 years old, in G4 (TDAP), the youngest patient had a 30 years old and the oldest had a 72 years old. In the comparison between the flap groups, the mean age in patients of G2 (CSMIF) was higher than that in G4 (TDAP). In this study, the mean age of PMMCF patients was 53.50 ± 9.1 years, the mean age of CSMIF patients was 63.00 ± 8.6 years, the mean age of RFFF patients was 53.52 ± 15.3 years and the mean age of TDAP patients was 46.60 ± 15.5 years **(Table 1).**

Regarding the sex parameter, In this study, there were 18 (43.9%) female patients and 23 (56.1%) male patients. In G1 (PMMCF), there were 5 females (50%) and 5 males (50%), in G2 (CSMIF), there were 7 females (70%) and 3 males (30%), in G3 (RFFF), there were 4 females (36.4%) and 7 males (63.6%) and in G4 (TDAP), there were 2 females (20%) and 8 males (80%) **(Table 1).**

In this study there were 19 (46.3%) smoking patients and 22 (53.7%) non-smoking patients. Regarding the smoking status among patients of G1 (PMMCF), there were 4(40%) smoking patients and 6 (60%) non-smoking patients, in patients of G2 (CSMIF), there were 6 (60%) smoking patients and 4 (40%) non-smoking patients, while in G3 (RFFF) there were 4 (36.4%) smoking patients and 7 (63.6%) non-smoking patients and in patients of G4 (TDAP), there were 5 (50%) smoking patients and 5 (50%) non-smoking patients **(Table 1).**

**Table 1: Socio-demographic Differences between Groups**

| Parameter | PMMCF (1) (n=10) | CSMIF (2) (n=10) | RFFF (3) (n=11) | TDAP (4) (n=10) | P-value |
|---|---|---|---|---|---|
| **Age/years** | 53.50 ± 9.1 | 63.00 ± 8.6 | 53.82 ± 15.3 | 46.60 ± 15.5 | = 0.053* |
| **P-value**** | 1 vs. 2 = 0.103 | 2 vs. 3 = 0.106 | 3 vs. 4 = 0.201 | 1 vs. 4 = 0.232 | |
| | 1 vs. 3 = 0.955 | **2 vs. 4 = 0.006** | | | |
| **Sex** | | | | | = 0.081*** |
| • **Female** | 5 (50%) | 7 (70%) | 4 (36.4%) | 2 (20%) | |
| • **Male** | 5 (50%) | 3 (30%) | 7 (63.6%) | 8 (80%) | |
| **Smoking Status** | | | | | = 0.628*** |
| • **Smoker** | 4 (40%) | 6 (60%) | 4 (36.4%) | 5 (50%) | |
| • **Non-smoker** | 6 (60%) | 4 (40%) | 7 (63.6%) | 5 (50%) | |

*ANOVA test was used to compare the mean difference between groups
**Post-hoc test with Bonferroni corrections
***Chi-square test was used to compare proportions between groups

Regarding the **TNM staging** of oral cavity tumors in our study, tumors had **$T_4$ stage** represented 30 (73.2%) cases: 10 (100%) of G1 (PMMCF), 10 (100%) of G4 (TDAP) patients, 7 (63.6 %) of G3 (RFFF) and 3 (30%) of G2 (CSMIF). tumors had $T_3$ stage represented 7 (17.1%) cases, tumors had $T_2$ stage represented 3 (7.34%) cases and tumors had $T_1$ stage represented only 1 (2.44%) case. Tumors had **N-stage ≥ $N_2$** represented 37 (90.3%) cases; 10 (100%) of G1 (PMMCF), 10 (100%) of G4 (TDAP) patients, 9 (90%) of G2 (CSMIF) and 8 (81.8 %) of G3 (RFFF). There was no tumors had M-Stage ≥ $M_1$ (as $M_0$ is an obligatory condition for all selected cases in this study) **(Table 2).**

The **level** of the cervical nodal involvement that was detected during preoperative clinical and radiological examination which was confirmed intraoperatively during performance of ND was level I in 6 (60%) patients of G1 (PMMCF) group, 5 (50%) patients of G2 (CSMIF) group, 1 (10%) patient of G4 (TDAP) group and not detected in patients of G3 (RFFF) group. The level was level I & II in 3 (27.3 %) patients of G3 (RFFF) group, 2 (20%) patients of G2 (CSMIF) group and not detected in any patient of G1 (PMMCF) group or G4 (TDAP) group. The level was level I, II & III in 7 (70%) patients of G4 (TDAP) group, 3 (27.3 %) patients of G1 (PMMCF), G2 (CSMIF) and G3 (RFFF) groups. The level was level I-V in 5 (45.45%) patients of G3 (RFFF) group, 2 (20%) patients of G4 (TDAP) group, 1 (10%) patients of G1 (PMMCF) group and not detected in any patient of G2 (CSMIF) group **(Table 2).**

**Table 2: Tumor Stage Differences between Groups**

| Parameter | PMMCF (1) (n=10) | CSMIF (2) (n=10) | RFFF (3) (n=11) | TDAP (4) (n=10) | P-value |
|---|---|---|---|---|---|
| **TNM Staging** | | | | | |
| • **T-stage (≥ 4)** | 10 (100%) | 3 (30%) | 7 (63.6%) | 10 (100%) | **= 0.001*** |
| • **N-stage (≥ 2)** | 10 (10%) | 9 (90%) | 8 (81.8%) | 10 (10%) | = 0.864 |
| • **M-stage (≥ 1)** | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | --------- |
| **Neck Lymph Node Side** | | | | | |
| • **No** | 0 (0%) | 0 (0%) | 0 (0%) | 1 (10%) | |
| • **Left** | 6 (60%) | 2 (20%) | 5 (45.5%) | 1 (10%) | **= 0.036*** |
| • **Right** | 3 (30%) | 7 (70%) | 1 (9.1%) | 5 (50%) | |
| • **Bilateral** | 1 (10%) | 1 (10%) | 5 (45.5%) | 3 (30%) | |
| **Neck Lymph Node Level** | | | | | |
| • **I** | 6 (60%) | 5 (50%) | 0 (0%) | 1 (10%) | |
| • **I, II** | 0 (0%) | 2 (20%) | 3 (27.3%) | 0 (0%) | **= 0.002*** |
| • **I, II, III** | 3 (30%) | 3 (30%) | 3 (27.3%) | 7 (70%) | |
| • **I, II, III, IV, V** | 1 (10%) | 0 (0%) | 5 (45.6%) | 2 (20%) | |

*Chi-square test was used to compare proportions between groups

**Intraoperative complications:**

The mean **operative time** of PMMCF cases was 200 ± 23.1 minutes with a range 180 - 240 minutes. The mean operative time of CSMIF cases was 199 ± 20.2 minutes with a range 180 - 250 minutes. The mean operative time of RFFF cases was 220 ± 19.2 minutes with a range 200 - 250 minutes. The mean operative time of TDAP cases was 212 ± 24.9 minutes with a range 180 - 250 minutes **(Table 3).**

According to the mean **intraoperative blood loss** in PMMCF and CSMIF cases was nearly equal (760 ± 68.6 ml in PMMCF cases versus 760 ± 61.8 ml in CSMIF cases). The mean intraoperative blood loss in RFFF cases was 872.27 ± 68.9 ml. The mean intraoperative blood loss in TDAP cases was 1020 ± 48.4 ml **(Table 3).** According to **intraoperative flap-related complications**, there was flap bulkiness occurred in 2 (20%) patients of G1 (PMMCF) group and 1 (10%) patient of G4 (TDAP) group. Flap ischemia occurred in 2 (20%) patients of G1 (PMMCF) group, 1 (10%) patient of G2 (CSMIF) group, 1 (9.1%) patient of G3 (RFFF) group and 1(10%) patient of G4 (TDAP) group **(Table 3).**

**Table 3: Intra-operative Sequence and Complications Differences between Groups**

| Parameter | PMMCF (1) (n=10) | CSMIF (2) (n=10) | RFFF (3) (n=11) | TDAP (4) (n=10) | P-value |
|---|---|---|---|---|---|
| **Operative Time/min.** | 200.00 ± 23.1 | 199.00 ± 20.2 | 220.00 ± 19.2 | 212.00 ± 24.9 | = 0.084* |
| **P-value**** | 1 vs. 2 = 0.919<br>**1 vs. 3 = 0.035** | **2 vs. 3 = 0.028**<br>2 vs. 4 = 0.192 | 3 vs. 4 = 0.358 | 1 vs. 4 = 0.228 | |
| **Blood Loss/ml** | 760.00 ± 68.6 | 760.00 ± 61.8 | 872.27 ± 68.9 | 1020.00 ± 48.4 | **= 0.019*** |
| **P-value**** | 1 vs. 2 = 1.000<br>1 vs. 3 = 0.208 | 2 vs. 3 = 0.208<br>2 vs. 4 = 0.103 | 3 vs. 4 = 0.103 | **1 vs. 4 = 0.006** | |
| **Intra-operative Complications** | | | | | |
| • **No** | 5 (50%) | 9 (90%) | 9 (81.8%) | 9 (90%) | **= 0.019***** |
| • **Bulky Flap** | 2 (20%) | 0 (0%) | 0 (0%) | 1 (10%) | |
| • **Ischemia** | 2 (20%) | 1 (10%) | 1 (9.1%) | 1 (10%) | |

*ANOVA test was used to compare the mean difference between groups
**Post-hoc test with Bonferroni corrections
***Chi-square test was used to compare proportions between groups

**Predictors of postoperative complications**

Regarding the predictors of postoperative complications among the studied cohort. Age, sex and smoking status of the patients and tumor N-stage, tumor grade, site of lesion and level of the involved cervical lymph nodes were not found to give a statistically significant liability for occurrence of complications. In the final multivariate regression model there were three predictors; type of flap, history of neoadjuvant CRTH and T-stage **(Table 4);**

For type of flap; TDAP flap were 2 times more liable for developing complications in comparison with PMMCF flap (AOR=1.9, 95%CI: 0.7–6.67, p-value <0.05) and his was statistically significant. RFFF were 1.3 times more liable for developing complications in comparison with PMMCF flap. Also CSMIF were 98% less liable for developing complications in comparison with PMMCF flap and his was statistically significant.

Patients with positive history of neoadjuvant CRTH are 52% less likely to developing complictions than those with negative history of neoadjuvant CRTH (AOR=0.53, 95% CI: 0.4–0.99, p-value <0.05) and this was statistically significant.

Likewise, patients with T4 stage had 1.7 times more risk for developing complications (AOR=1.67, 95% CI: 1.03–3.21, p-value <0.05) and this was statistically significant.

**Table 4: Predictors of Disease Complications among the studied Cohort**

| Variable | Univariate | | Multivariate | |
|---|---|---|---|---|
| | OR (95% CI) | P-value | OR (95% CI) | P-value |
| **Age/years** | 1.011 (0.959–1.065) | = 0.687 | | |
| **Sex (Male)** | 0.536 (0.125–2.290) | = 0.400 | | |
| **Type of Flap** | | | | |
| • **PMMCF** | 1 | **= 0.044** | 1 | **= 0.040** |
| • **CSMIF** | 0.540 (0.639–17.761) | = 0.195 | **0.191 (1.009–12.724)** | **= 0.045** |
| • **RFFF** | **1.530 (1.516–29.754)** | **= 0.047** | **1.354 (1.516–29.754)** | **= 0.046** |
| • **TDAP** | **4.000 (0.414–8.146)** | **= 0.26** | **2.041 (0.698–6.658)** | **= 0.031** |
| **Smoking** | 1.879 (0.596–4.245) | = 0.479 | | |
| **History of CRTH** | **0.464 (0.213–0.998)** | **= 0.049** | **0.477 (0.395–0.987)** | **= 0.049** |
| **T-stage (= 4)** | **2.509 (1.091–4.648)** | **= 0.044** | **1.687 (1.034–3.210)** | **= 0.039** |
| **N-stage (≥ 2)** | 1.128 (0.684–5.164) | = 0.572 | | |
| **Differentiation (Poor)** | 1.138 (0.941–3.077) | = 0.098 | | |
| **Grade (II)** | **1.093 (1.005–4.118)** | **= 0.017** | **1.405 (1.011–5.101)** | **= 0.041** |

**OR, Hazard Ratio; CI, Confidence Interval**

**Early postoperative complications:**

Regarding to early short term complications for the patient during follow up period (postoperative **first 4 weeks**) as:

**Blood loss** in drain, the mean postoperative blood loss in PMMCF cases was 180 ± 91.4 ml, in CSMIF cases was 94.44 ± 15.2 ml, in RFFF cases was 110 ± 12.6 ml and in TDAP cases was 105.65 ± 15.9 ml **(Table 5**).

The postoperative **hospital stay**, the mean postoperative hospital stay in PMMCF cases was 11.7 ± 1.8 days, in CSMIF cases was 10.8 ± 1.2 days, in RFFF cases was 14.45 ± 2.5 days and in TDAP cases was 22.67± 8.4 days **(Table 5).**

The postoperative **ICU stay**, the mean postoperative ICU stay in PMMCF cases was 0.4 ± 0.3 days, in CSMIF cases was 1.1 ± 0.7 days, in RFFF cases was 2.09 ± 0.3 days in TDAP cases was 1.67± 0.3 days **(Table 5).**

**Table 5: Early Short-term (1st 4weeks Post-operative) Complications Differences between Groups**

| Parameter | PMMCF (1) (n=10) | CSMIF (2) (n=10) | RFFF (3) (n=11) | TDAP (4) (n=10) | P-value |
|---|---|---|---|---|---|
| **Blood Loss in Drain** | 180.00 ± 91.4 | 94.44 ± 15.2 | 110.00 ± 12.6 | 105.65 ± 15.9 | = 0.605* |
| **P-value**** | 1 vs. 2 = 0.234<br>1 vs. 3 = 0.316 | 2 vs. 3 = 0.827<br>2 vs. 4 = 0.879 | 3 vs. 4 = 0.950 | 1 vs. 4 = 0.300 | |
| **Hospital Stay/days** | 11.70 ± 1.8 | 10.80 ± 1.2 | 14.45 ± 2.5 | 22.67 ± 8.4 | = 0.061* |
| **P-value**** | 1 vs. 2 = 0.875<br>1 vs. 3 = 0.623 | 2 vs. 3 = 0.515<br>**2 vs. 4 = 0.050** | 3 vs. 4 = 0.160 | 1 vs. 4 = 0.069 | |
| **ICU Stay/days** | 0.40 ± 0.3 | 1.10 ± 0.7 | 2.09 ± 0.3 | 1.67 ± 0.3 | **= 0.010*** |
| **P-value**** | 1 vs. 2 = 0.071<br>**1 vs. 3 = 0.009** | 2 vs. 3 = 0.101<br>2 vs. 4 = 0.183 | 3 vs. 4 = 0.303 | **1 vs. 4 = 0.044** | |

*ANOVA test was used to compare the mean difference between groups

**Post-hoc test with Bonferroni corrections

***Chi-square test was used to compare proportions between groups

**Cosmetic outcome:**

Regarding cosmetic outcome or social **acceptance**, it was satisfactory in 6 patients in G2 (CSMIF) and G3 (RFFF) groups, in 4 (40%) patients in G1 (PMMCF) group and in 3 (30%) patients in G4 (TDAP) group. It was fair in 4 patients in G2 (CSMIF) and G4 (TDAP) groups, in 3 (30%) patients in G1 (PMMCF) group and in 2 patients in G3 (RFFF) group. It was dissatisfactory in 3 patients in G1 (PMMCF), G3 (RFFF) and G4 (TDAP) groups **(Table 6).**

**The flap suitability** to cover the defect; this suitability had been detected over 12- 24 months of postoperative follow-up period, the flap was suitable for defect coverage in 6 (60%) patients in G1 (PMMCF), G2 (CSMIF) and G4 (TDAP) groups, and in 5 (47.5%) patients in G3 (RFFF) group. The flap was oversized in 3 patients in G4 (TDAP), 2 patients in G1 (PMMCF) and only 1 (10%) patient in G1 (PMMCF) and G3 (RFFF) groups group. The flap was less suitable for defect coverage in 1 patient in G2 (CSMIF) and G3 (RFFF) groups **(Table 6).**

Regarding to the mean percentage of **flap volume reduction (FVR)** which is measured clinically and radiologically estimated via MRI, follow-up of our patients showed a FVR of 29.5 ± 11.2 in 6 patients in RFFF group with one patient of this group had a FVR of 50%, 29.29 ± 9.4 in 5 patients in PMMCF group, 25.65 ± 13.3 in 6 patients in TDAP group and 25.56 ± 9.2 in 5 patients in CSMIF group **(Table 6).**

The effect of **adjuvant Chemoradiotherapy** (CRTH) on the flap, there was no effect in 6 patients on G2 (CSMIF), G3 (RFFF) and G4 (TDAP) groups and on 5 patients in G1 (PMMCF) group. There was mild effect (the effect was in the form of flap contracture) on 3 patients in G2 (CSMIF), G3 (RFFF) and G4 (TDAP) groups and on 2 patients in G1 (PMMCF) group **(Table 6).**

**Table 6: Late Short-term (12-24 months Post-operative) Complications Differences between Groups**

| Parameter | PMMCF (1) (n=10) | CSMIF (2) (n=10) | RFFF (3) (n=11) | TDAP (4) (n=10) | P-value |
|---|---|---|---|---|---|
| **Flap Suitability for Defect Coverage** | | | | | |
| • **Suitable** | 6 (60%) | 6 (60%) | 5 (47.5%) | 6 (60%) | = 0.394* |
| • **Oversized** | 2 (20%) | 1 (10%) | 1 (9.1%) | 3 (30%) | |
| • **Less Suitable** | 0 (0%) | 1 (10%) | 1 (9.1%) | 0 (0%) | |
| **Volume Reduction %** | 29.29 ± 9.4 | 25.56 ± 9.2 | 29.50 ± 11.2 | 25.65 ± 13.3 | |
| **P-value*** ** | 1 vs. 2 = 0.514<br>1 vs. 3 = 0.969 | 2 vs. 3 = 0.449<br>2 vs. 4 = 0.998 | 3 vs. 4 = 0.449 | 1 vs. 4 = 0.514 | = 0.792** |
| **Effect of CRTH on Flap** | | | | | |
| • **None** | 5 (50%) | 6 (60%) | 6 (55.6%) | 6 (60%) | = 0.413* |
| • **Mild** | 2 (20%) | 3 (30%) | 3 (27.3%) | 3 (30%) | |
| • **Moderate** | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | |
| • **Severe** | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | |

*Chi-square test was used to compare proportions between groups
*ANOVA test was used to compare the mean difference between groups
**Post-hoc test with Bonferroni corrections

## DISCUSSION

The current study showed that all SMIF cases were harvested from the tumor contralateral side, to stand on the hypothesis that CSMIF is better than ipsilateral submental island flap or not regarding or aiming at improvement of the oncologic outcome in our future patients not involved in this study.

RFFF is very useful flap for soft tissue intra-oral reconstruction. The vascular territory is reliable and offers significant versatility as either a fasciocutaneous, fascial, or osteocutaneous flap [7]. RFFF is relatively easy to raise from the volar region of the forearm. RFFF has pliable skin paddle, relatively hairless with less bulk spreads over shapes of Oral cavity, and has good success rates [9, 10].

**Angrigiani *et al.* [8],** described the TDAP flap, which is based on perforators arising from the thoracodorsal artery and utilizes the overlying skin but not the underlying LD muscle. The TDAP flap therefore shares the benefits of long pedicle length and broad large surface area, yet has the additional advantages of reduced thickness and decreased morbidity when

comparison is made to the LD flap [11]. The TDAP flap is not widely used in head and neck surgery. It possesses all of the characteristics of the ideal flap described by Lyons for soft tissue reconstruction of the head and neck [12].

In our study regarding to PMMCF cases, the average age of the patients was ranged from 37 to 66 years old (i.e. from 4th to 7th decades), there were 5 females (50%) and 5 males (50%) and there were 4(40%) smoking patients and 6(60%) non-smoking patients.

Regarding to CSMIF cases, the average age of the patients was ranged from 50 to 78 years old (i.e. from 6th to 8th decades), there were 7 females (70%) and 3 males (30%) and there were 6 (60%) smoking patients and 4(40%) non-smoking patients. In our study regarding to RFFF cases, the average age of the patients was ranged from 27 to 68 years old (i.e. from 3th to 7th decades), there were 4 females (36.4%) and 7 males (63.6%) and there were 4 (36.4%) smoking patients and 7 (63.6%) non-smoking patients. In our study regarding to TDAP cases, the average age of the patients was ranged from 30 to 72 years old (i.e. from 4th to 8th decades), there were 2 females (20%) and 8 males (80%) and there were 5(50%) smoking patients and 5(50%) non-smoking patients.

According to the clinical history of neoadjuvant therapy, there was a significant difference between the four groups; in which 4 (40%) patients of G4 (TDAP), 2 (20%) patients of G1 (PMMCF) showed a positive history of neoadjuvant radiotherapy while no patient of G2 (CSMIF) or G3 (RFFF) showed a positive history of neoadjuvant radiotherapy. 6 (60%) patients of G1 (PMMCF), 1 (10%) patient of G1 (CSMIF), 1 (9.1%) patient of G3 (RFFF) and 4(40%) patients of G4 (TDAP) showed a positive history of neoadjuvant chemotherapy.

According to the site of oral cavity tumor, in our study the most common site of tumor was located at buccal (cheek) region in 21 (51.2%) patients (gave a significant value about 0.029), followed by 11 patients had the tumor at tongue (also gave a significant value about 0.020), 8 patients had the tumor at gingival mucosa, 6 patients had the tumor at lip, 5 patients had the tumor at FOM and 3 patients had the tumor at the palate. This results matching with study done and also documented that the commonest site of cancer was buccal mucosa [13].

Regarding to the defect type, it was occurred mainly in mucosa and muscle (MM), occurred in 15 patients (36.6%), followed by defects occurred in mucosa, muscle, bone and skin (MMBS) that occurred in 10 patients (24.4%), then defects that occurred in mucosa, muscle and skin (MMS) that occurred in 9 patients (21.9%), then mucosa, muscle and bone (MMB) that occurred in 7 patients (17.1%). Other studies reported different results regarding to the defects, one of them showed that the defects was in oral mucosal only in 65% of the patients **Gupta *et al.*** [14] and another demonstrated that the defect mainly was in the tongue and intraoral region [15].

Regarding the TNM staging of oral cavity tumors in our study, tumors had T4 stage represented in 30 (73.2%) cases and this gave a significant value ($p = 0.001$). Another study reported that the major number of the patients (43%) had T**4** stage of the tumor [13]. Another study also reported that100% of their patients had T-stage 4 [16]. In our study tumors had N-stage $\geq N_2$ represented in 37 (90.3%) cases, there was no tumors had M-Stage.

The **level** of the cervical nodal involvement that was detected during preoperative clinical and radiological examination which was also had been confirmed intraoperatively during performance of ND was mainly at level I-III, that occurred in 16 ( 40%) patients, followed by level I, occurred in 12 (30%) patients, then level I-V, occurred in 8(20%) patients and at level I,II, occurred in 5 (12.5%) patients. These results gave a significant value, another study done who found an incidence of level I involvement to be 66.7% [17]. In contrast, few authors have reported that level II was the most commonly involved site for neck metastases [18]. Moreover, in other study, level IV involvement in oral cancer alone was seen in around 10% of cases [19]. This different presentation of lymph node involvement could be attributed to varied pattern of lymphatics in individual neck and anatomical distribution of lymphatics [20].

According to **intraoperative flap-related complications**, there was flap bulkiness occurred in only 2 (20%) patients of G1 (PMMCF) group and 1 (10%) patient of G4 (TDAP) group. Flap ischemia occurred in 2 (20%) patients of G1 (PMMCF) group, 1 (10%) patient of G2 (CSMIF) group, 1 (9.1%) patient of G3 (RFFF) group and 1(10%) patient of G4 (TDAP) group. These complications not matching with **Tornero *et al.*** [21] which reported that, they had not intraoperative complications [21]. According to postoperative complications, the largest volume of blood loss occurred in drain with PMMCF, longest stay time at hospital occurred with TDAP, the longest period of ICU stay occurred with RFFF.

Regarding to postoperative **recipient site complications** during early short-term postoperative follow-up period,

In the patients of G1 (PMMCF) group, we reported seroma in 3 (30%) patients, hematoma in 3 (30%) of the patients, 20% of the patients with wound infection, 10% of the patients with wound dehiscence and 10% of patients with delayed wound healing. Another recipient site complication as necrosis, infection, dehiscence and fistulization and rare complications as osteomyelitis reported by another study [22].

In patients of G2 (CSMIF) group, 10% of the patients had hematoma, 10% of the patients had seroma, 10% of the patients had wound dehiscence, 10% of the patients had wound infection and 10% of the patients had delayed wound healing.

In patients of G3 (RFFF) group, 9.1% of the patients had wound dehiscence and 9.1 % of the patients had wound infection. Another study reported recipient site complications in 24%of their patients, 8% were severe in form of total flap loss and 16% were minor as Fistula, dehiscence and hematoma [(23)].

In patients of G4 (TDAP) group, 20% of the patients had hematoma, 20% of the patients had wound dehiscence, 20% of the patients had wound infection and 10% of the patients had delayed wound healing.

In our study, we reported **the cosmetic outcome** as following**;**

It was satisfactory in 19 (46.34%) patients, fair in 13 (31.71%) patients and dissatisfactory in 9 (21.95%) patients.

**The flap suitability** to cover the defect had been detected over 12- 24months of postoperative follow-up period, the flap was suitable for defect coverage in 6 (60%) patients in G1 (PMMCF), G2 (CSMIF) and G4 (TDAP) groups, and in 5 (47.5%) patients in G3 (RFFF) group. The flap was oversized in 3 patients in G4 (TDAP), 2 patients in G1 (PMMCF) and only 1 (10%) patient in G1 (PMMCF) and G3 (RFFF) groups group. The flap was less suitable for defect coverage in 1 patient in G2 (CSMIF) and G3 (RFFF) groups.

**Flap volume reduction (FVR)** which is measured clinically and radiologically estimated via MRI, follow-up of our patients showed a FVR of 29.5 ± 11.2 in 6 patients in RFFF group with one patient of this group had a FVR of 50%, 29.29 ± 9.4 in 5 patients in PMMCF group, 25.65 ± 13.3 in 6 patients in TDAP group and 25.56 ± 9.2 in 5 patients in CSMIF group**.** The FVR usually results from muscle atrophy caused by muscle denervation and fat tissue shrinkage over time and usually assessed by CT volumetry [(24)]**.** Another study done by **Sakamoto *et al.*** where they used MRI volumetry, that study showed approximately 30% FVR [(25)]**.**

The effect of **adjuvant Chemoradiotherapy** (CRTH) on the flap, there was no effect in 6 patients on G2 (CSMIF), G3 (RFFF) and G4 (TDAP) groups and on 5 patients in G1 (PMMCF) group. There was mild effect (the effect was in the form of flap contracture) on 3 patients in G2 (CSMIF), G3 (RFFF) and G4 (TDAP) groups and on 2 patients in G1 (PMMCF) group**.** Two wat ANOVA analytic studies reported that the CRTH has variable effects (according to the given doses) on the flap perfusion using Luna fluorescence angiography [(26)]**.**

## CONCLUSION

It could be concluded that the chosen 4 flaps for this study are applicable to be used for post ablative oral cavity reconstruction, but TDAP flaps were found to be 2 times more liable for risk of complications than PMMCF flaps while RFFF flaps were found to be 1.3 times more liable for risk of complications than PMMCF flaps. CSMIF flaps showed a 58% less liability for developing clinically or radiologically detectable LRF/LRR and showed no mortalities. LRF/LRR was more with TDAP flaps (2.6 times more risk or liability for LRF/LRR than PMMCF) followed by RFFF flaps (1.2 times more risk or liability for LRF/LRR than PMMCF).

CSMIF showed 58% less risk of LRF/LRR than PMMCF. Flap failure or loss was detected mainly in TDAP flaps RFFF flaps (each showed 1.2 times more liable for risk of flap failure than PMMCF flaps). Infection is the most common risk factor of flap insult, ischemia and finally failure or loss.

Our flaps were equal in suitability for defect coverage (50-60%). Functional outcomes were better with CSMIF then with RFFF, and these outcomes were worse with TDAP, oncologic outcomes were better with CSMIF and cosmetic outcomes were better in CSMIF and RFFF cases. Relatively, TDAP flap cases were higher than others in the overall care costs.

## RECOMMENDATIONS

- Almost always follow the reconstructive ladder for coverage of oral cavity defects and do not jump from lower to higher options except in very few cases which have special circumstances.
- When SMIF is an ideal reconstructive option, contralateral flaps will be strongly recommended to decrease the risk of LRF/LRR (and to have a better oncologic outcome than ipsilateral flaps). In our study, contralateral flaps had a lower risk of LRF/LRR although they were used to reconstruct moderately undifferentiated (in 30% of our CSMIF cases) and poorly undifferentiated (in 20% of our CSMIF cases) tumors.
- CSMIF are recommended to cover defects in anterior portions of oral cavity while RFFF are recommended for coverage of posteriorly situated defects and palatal ones.

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