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LONG TERM FUNCTIONAL AND ESTHETIC OUTCOMES AFTER FIBULA FREE FLAP RECONSTRUCTION OF THE MANDIBLE.:

(Physician assessed and patient reported outcomes)

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Abstract

Objectives: To report functional and esthetic outcomes, after fibula free flap (FFF) reconstruction of the mandible for oral cancer, assessed by physicians, non-clinicians and patients.

Materials and Methods: Twenty-five long term survivors from oral cancer after FFF reconstruction were recalled for head and neck examination by surgeons, for photographs and patient reported outcomes, using EORTC, QLQ C-30, H&N –35 and FACE Q questionnaires.

Results: Physicians reported 64% restoration of functionality compared to normal. Patients reported high scores on QLQ-C30, but lower scores on H&N-35. Esthetic scores were reported higher by clinicians than non-clinicians. The decline in function and appearance was attributed to loss of lower dentition, trismus, mal occlusion, xerostomia and tissue atrophy.

Conclusion: To minimize the decline in function and appearance, immediate dental implants in FFF, better reconstruction of the temporomandibular joint, newer methods of radiotherapy to minimize xerostomia and oral exercises to prevent trismus should be considered.

Keywords

Oral cancer; head and neck cancer; fibula free flap; functional outcomes; esthetic outcomes; Quality of life; long term survivors; patient reported outcomes; xerostomia; trismus; malocclusion; QLQ C-30; QLQ HN-35; FACE Q

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CONFLICT OF INTEREST STATEMENT: None declared.

INTRODUCTION

Oral Cancer is one of the most frequently encountered malignancies in the head and neck region. Each year nearly half a million people are diagnosed with oral cancer worldwide . A significant proportion of these patients present with advanced stage disease. Early invasion of the mandible occurs most commonly from primary cancers of the alveolus or lower gum. However, lower gum (mandible) is not the most commonly encountered primary site in the oral cavity. Invasion of the mandible by advanced stage tumors of the floor of the mouth, tongue or buccal mucosa is not uncommon. These patients often require resection of a segment of the mandible, either due to direct tumor invasion or, due to extensive soft tissue disease contiguous to the mandible, to accomplish 'complete' resection of the primary tumor. The functional and esthetic sequelae of mandible resection are significant, if not devastating, and are life-long. In the past, reconstruction of the mandible was often not considered a priority, and a simple primary closure of the surgical defect was performed (1). Such patients had an unacceptable esthetic deformity and suboptimal restoration of oral function. In other patients, when mandible reconstruction was attempted, either with a metallic reconstruction plate, or non-vascularized bone graft, the results were far from satisfactory, both from an esthetic and a functional point of view (2,3,4,5).

Development of microsurgery, and the introduction of vascularized free flaps revolutionized the field of reconstructive surgery in the head and neck (6). Reconstruction of segmental mandibulectomy defects has been reported with a variety of free vascularized bone flaps such as the iliac crest, metatarsal, fibula, scapula and radius bones. The fibula free flap (FFF), first introduced by Taylor and later popularized by Hidalgo, is generally considered to be the gold standard for mandible reconstruction(7). In the immediate post-operative period, aesthetic results following FFF reconstruction are quite good. However, the recovery of all oral functions from such reconstruction has not been studied well. Furthermore, over time, bone and soft tissue atrophy can take place, causing deterioration in esthetic appearance and function as well. This is exacerbated in patients who receive post operative radiotherapy or chemo radiotherapy. Furthermore, as years go by, the natural aging process causes further deterioration in the esthetic appearance in long term survivors. While immediate esthetic results after FFF reconstruction are excellent, functional restoration of malocclusion, and other oral functions such as restoration of dentition/mastication, oral competency, lip support and ability to consume all types of food have not been studied well. Previous reports have evaluated functional outcome only from the patient's point of view, measuring their perceptions rather than using observer-rated testing(8,9). These subjective observations have not been compared with objective assessment by physicians. In addition, esthetic outcomes have not been compared between assessments by physicians and lay persons, to see how the patient is perceived in society. King et al reported on comparison of functional and esthetic outcomes following reconstruction with free flaps containing vascularized bone or soft-tissue alone(10). Several retrospective studies have reported on outcomes of mandible reconstruction with FFF. However, most of these focus on viability of the flap and immediate esthetic outcomes (11). Hidalgo et al. published a 10 year follow up study of 84 patients undergoing FFF reconstruction by him over a four year period to assess functional and esthetic outcomes.. Of these only 36 were alive. Six were living overseas and not

available for follow up. Of the remaining 30, twenty agreed to participate in their study and only 14 were available for physical examination. Others responded by telephone interviews. (8). This study underscores the difficulties in having a large number of patients available for long term studies. Many patients have advanced stage disease, or are elderly, and either die of their disease or due to other causes. Thus longer term follow-up studies with a large number of patients are difficult to conduct particularly in patients with advanced stage oral cancer, due to a limited number of patients surviving with control of their cancer. Or others dying from intercurrent disease.

The purpose of this study is to evaluate long term functional and esthetic outcomes after FFF reconstruction of all surviving patients with oral cancer treated at a tertiary care cancer center over the past 26 years. Our study includes, patient reported outcomes, physician assessed functional and esthetic outcomes, and lay person assessed esthetic outcomes. We also report the impact of radiotherapy (RT) on soft tissue and bone atrophy in the long term.

MATERIAL AND METHODS

The aim of this study is to assess long-term functional and esthetic outcomes after segmental mandibulectomy and FFF reconstruction from the patient, physician and lay person perspectives (public perception). Secondary objectives were to assess the relationship between time since reconstruction and progressive deterioration of functional and aesthetic outcomes, and finally the impact of post operative radiotherapy on the extent of bone and soft tissue atrophy and deterioration of function and esthetic appearance.

After obtaining approval by the Memorial Sloan Kettering Cancer Center (MSK) Institutional Review Board (MSK#15–244), a retrospective chart review was conducted on all patients who underwent segmental mandibulectomy and FFF reconstruction on the Head and Neck Service at MSK from 1987 to 2013. The inclusion criteria were that they were able to read and write in the English language since the questionnaires required by the protocol are available only in English, and they were able to travel to the MSK outpatient clinic or have access to email, the MSK patient portal and a computer with a camera for the follow up examination by a physician and completion of the questionnaires. As a token of appreciation, patients who agreed to participate in the study were given a “gift card” to compensate for their traveling expense. Patients who had marginal mandibulectomy, or segmental mandibulectomy with any other type of reconstruction, or no reconstruction were excluded from this study. All patients were required to sign an informed consent to participate in the study.

A total of 416 patients underwent FFF reconstruction of the mandible during this time period. Patients who died from any cause, and/or were lost to follow-up (355), were excluded. Only 61 patients were eligible to participate in this prospective study. Five patients from foreign nations unable to return for examination and 31 patients who declined participation in the study were also excluded. This left only 25 eligible patients who all signed consent to participate in the study. All included patients received an introductory letter about this study, followed by a phone call to answer their questions and requesting them to participate in this study. All patients were encouraged to come for a physical

examination by a clinician. Those who were unable to come due to long distance from their home to our center were offered an option to complete enrollment by mail/ e mail /phone and a video conference call by the senior investigator. Although not equivalent to a in person physical examination, the required observations for assessment of esthetic appearance and function, such as mouth opening, jaw deviation, tissue atrophy etc., could be adequately evaluated by a live video call, and thus these patients were included in the study. .

Evaluation of long-term functional and esthetic outcomes by a clinician:

The functional outcome was assessed with a questionnaire, and the esthetic outcome was judged by two independent observers. In our study, we assessed outcomes based on both the patient and physician points of view over an extended period since reconstruction (from ~2 to 28 years). The treating surgeon, or the surgeon's designee (Fellow) performed a physical examination of the head and neck region. If the patient chose to participate in the study by video conference they were interviewed by the senior investigator on that video call. The examining physician then completed an 11-item form, first described by Rogers et al, for evaluation of oral function,(12). This examination assessed appearance, lip competence, tongue movement, oral mucosa, dental state, mouth opening, speech, drooling, diet, oral sensation, and shoulder movement. The 11-item clinical examination was scored according to the original validation study by Rogers to yield a total score ranging from 0 to 29, with higher scores indicating better function (13).

We also evaluated an objective visual assessment method for esthetic outcome from the clinician perspective (as well as from the perspective of a lay person (non-clinician research staff). Patient photographs were taken by one of the investigators at the end of the interview. 4 photos were taken: en face in repose, en face with open mouth, left profile, and right profile. Archived photographs from the early post-operative period were used for comparison with the photos taken during the interview. For each patient, 3 clinicians and 3 non-clinical staff reviewed the early post-operative and current photo sets separately and rated each set on the following 3 characteristics on a scale from 1 ("Poor") to 4 ("Excellent"): overall appearance, symmetry of soft tissues in the lower third of the face, and jaw deviation with open mouth. For each patient, and for each of the 3 characteristics, the mean clinician rating was calculated separately for the early post-operative and current photo ratings. The post-operative ratings were subtracted from the current ratings to index change in clinician-rated appearance. The ratings from the 3 non-clinicians were similarly processed to produce the non-clinician esthetic rating endpoints. The comparison of the photograph assessment was anonymous. Both the clinicians and non-clinicians were not aware of the patient's history, name, demographics, the type of surgery or reconstruction.

Evaluation of Esthetic Outcomes by a lay person:

Three non-clinical persons were chosen as lay persons. They were given photographs of all patients anonymously to compare and score their assessment on a short questionnaire. The first set of pictures were early post-operative photographs within 6 months of surgery retrieved from the archives of the Plastic and Reconstructive surgery service at MSK. Study photographs were taken at the time of their clinical evaluation at follow up. Four pictures were taken. A frontal view with mouth closed, mouth open and right and left lateral views.

Evaluation of patients' perception of their long-term Quality of Life and functional outcomes, symptoms, and esthetic outcomes:

The quality of life and functional outcome of head and neck cancer patients was measured using the European Organization for Research and Treatment of Cancer (EORTC) core quality of life questionnaire (EORTC QLQ-C30, v3) and its head and neck cancer-specific module (EORTC OLQ H&N-35) (14,15). We also utilized the FACE-Q Oncology Module: Mandibulectomy, a new patient-reported outcome measure which was used to evaluate patient perception of their esthetic outcomes. (16,17) It also has functioning-related subscales that were used to supplement the functional information provided by the EORTC measures. Specifically, four FACE-Q scales assessed patients' esthetic outcomes in terms of their (1) appraisal of their smile, (2) satisfaction with their smile, (3) appraisal of facial appearance, and (4) satisfaction with facial appearance.

Statistical Methods:

Demographics, physical findings, and clinician and patient-reported outcomes were summarized using descriptive statistics. Means and 95% confidence intervals (CIs) were plotted for continuous variables. Categorical variables were summarized using frequency counts and percentages. Pearson correlation coefficients were calculated to quantify the impact of time since reconstruction on the various functional and esthetic outcomes (from the patient, clinician, and non-clinician perspective). We used paired t-tests to evaluate whether the ratings of the archived early post-operative photos were significantly different from the ratings of the new photos taken at study assessment.

RESULTS

Study Population

The median age of patients in the study group was 60–2 years (range, 40–85 years) and 72% were male. The majority of patients (56%) had their primary tumor involving the lower alveolus or lower gum. The histological diagnosis in over three quarters of the patients (76%) was squamous cell carcinoma (SCC). The others had adenoid cystic carcinoma, myoepithelial carcinoma of minor salivary gland, recurrent odontogenic keratocyst, osteogenic sarcoma and verrucous carcinoma. Fifty-six percent of patients had higher stage primary tumors (c T3–4), and one fifth (20%) had clinically N+ disease.

Patient Reported Outcomes

Patient-reported esthetic and functional outcomes are summarized in Figure 1. On the FACE-Q, patients reported higher appraisal of and satisfaction with their smile than with their overall facial appearance. For both smile and facial appearance, patients' appraisals were generally lower than their satisfaction levels.

Patients generally reported high levels of function on the QLQ-C30 functional scales (Figure 2), with all functional scale score means larger than 74 on the 0 to 100 score range. The lowest functional scores were reported for Global health status/QoL (QoL- mean = 74.2, interquartile range, IQR=35.5) and the highest for Physical functioning (PF- mean = 91.7, IQR=6.7). Scores on QLQ-C30 general symptom scales were relatively low, with highest

scores for Insomnia (SL- mean = 22.2, IQR=33.3) and Constipation (CO- mean = 18.1, IQR=33.3) and lowest scores for Nausea/Vomiting (NV- mean = 1.4, IQR=0) and Diarrhea (DI mean = 2.8, IQR=0).

The symptom scales on the QLQ-H&N35, which index symptoms specific to patients with head & neck cancers, were comparatively higher than the more general QLQ-C30 symptom scores. The highest QLQ-H&N35 scores were for Dry mouth (HNDR- mean = 49.3, IQR=100), Teeth (HNTE- mean = 38.9, IQR=75), Opening mouth (HNOM- mean = 38.7, IQR=66.7), Less sexuality (HNSX- mean = 36.0, IQR=66.7) and Sticky saliva (HNSS- mean = 36, IQR=0). The lowest QLQ-H&N35 scores were Felt ill (mean = 8.0) and Trouble with social contact (HNSC; mean = 11.7, IQR =13.3). On the 5 yes/no QLQ-H&N35 questions, 1 (4%) patient reported using a feeding tube, 3 (12%) used pain killers, 5 (20%) gained weight, 7 (28%) had taken nutritional supplements, and 8 (32%) lost weight.

Clinician and Non Clinician Reported Outcomes

The physician-completed 11-item clinical examination had a mean (95% CI) score of 18.4 (16.5–20.3). This corresponds to approximately 64% of the maximum possible score of 29 (which represents perfect function). The majority of findings which had a negative impact on functional outcomes were related to absence of mandibular teeth, xerostomia, trismus, malocclusion and loss of sensation of the lower lip.

Clinician and non-clinician esthetic ratings of post-operative and current photographs of patients are summarized in Figure 2. All current ratings were significantly lower than early post-operative ratings ($p < 0.05$) except for the non-clinician ratings of jaw deviation ($p = 0.75$). As can be seen in Figure 3, the decreases in ratings of post-operative vs current photographs were greater among clinicians than non-clinicians. Clinicians rated all features significantly higher than non-clinicians at both time points (all $p < 0.01$), with these differences most pronounced for the early post-operative ratings.

The time since reconstruction ranged from 1.6 to 16.9 years, with a median (25th–75th percentile) of 7.9 (4.2–11.8) years. Time since reconstruction was significantly correlated with FACE-Q Appraisal of Smile (Pearson's $r = 0.71$, $p < 0.01$) and QLQ-H&N35 Less Sexuality ($r = -0.59$, $p < 0.01$), with patients having more positive smile appraisals and fewer reports of sexual symptoms with longer time since reconstruction. Patients also reported worse Physical Functioning ($r = -0.48$, $p < 0.05$) and increased loss of appetite ($r = 0.49$, $p < 0.05$) on the QLQ-C30 with greater time since reconstruction. These symptoms can also be attributed in part to the normal aging process.

Effect of radiotherapy (RT)

Nineteen out of the 25 patients had post operative RT. There were no significant differences on any of the variables by RT status. For the PROs, patients who received RT, tended to have better function and fewer symptoms on the QLQ-C30, but they tended to have more symptoms than non-RT patients on the QLQ-H&N35. The non-RT patients tended to have their pictures rated more favorably than the RT patients, but the differences were small and not statistically significant (Table 1).

DISCUSSION

There are only few studies in the literature that report the quality of life and functional outcomes after mandibulectomy and reconstruction with FFF(11,18,19,20). According to our review to date, there have been no studies with more than 14 patients to report such outcomes 18 months after surgery(8). Our study reviewed a large series of patients over a long period of time at a tertiary care cancer center, who underwent FFF reconstruction following segmental mandibulectomy for oral cancer. In order to report outcomes in a cancer population, we restricted our study to majority of patients with malignant tumors in the oral cavity. To attain objectivity, we elected to have three separate means of evaluation of function and esthetics; 1) Patient reported outcomes, 2) Physician assessed outcomes and 3) lay person assessed esthetic outcomes, to reflect public perception of the patient's image. The quality of life and functional outcome of head and neck cancer patients was measured using the European Organization for Research and Treatment of Cancer (EORTC) core quality of life questionnaire (EORTC QLQ-C30, v3) and its head and neck cancer-specific module (EORTC H&N-35). These questionnaires have demonstrated good acceptability, internal consistency reliability, test-retest reliability, and high responsiveness. The EORTC questionnaires have also demonstrated good convergent validity with the UWQOL, which addresses many important aspects of the head and neck cancer patient experience, have undergone thorough development and validation, and represent robust alternatives to the UWQOL. We also utilized the FACE-Q Oncology Module-Mandibulectomy, a new patient-reported outcome measure which was used to evaluate patient perception of their esthetic outcomes. It also has functioning-related subscales that was used to supplement the functional information provided by the EORTC measures.

For physician assessment we used Rogers clinical questionnaire of 11 items, and for lay person assessment we used early post-operative photographs and study photographs for comparison.

It is well known that with passage of time and increasing age, esthetic appearance of the face in general and the reconstructed tissues in particular will deteriorate. An extreme example of progressive soft tissue and bone atrophy is seen in a patient, who underwent anterior arch resection for locally advanced lymphoma involving the mandible and a composite fibula free flap reconstruction. Compared to the early post-operative appearance, progressive atrophy is seen at 5 and 10 years post-surgery(Figure43). However, this degree of atrophy is generally not seen in non-radiated patients, except for esthetic changes related to normal aging process(Figure4). On the other hand, atrophic changes are exacerbated in patients who receive post-operative radiotherapy. Soft tissue atrophy may be seen as early as 2 to 4 years after radiotherapy(Figure 5 and Figure6). This leads to progressive decline in function and esthetic appearance. Normal aging process further adds to the deterioration in all domains of function and esthetics. Thus, these factors have to be considered in assessing function, esthetics and overall quality of life in long term survivors after FFF reconstruction of the mandible.

On the 11 item functional assessment by physicians, most of the lower scores recorded by clinicians were related to the absence of teeth in the reconstructed lower jaw, reduced mouth

opening (trismus) and malocclusion (deviation of the jaw on opening mouth). Further, xerostomia in radiated patients, and loss of sensation of the lower lip added to functional decline, giving only a 64% functional recovery score by clinicians.

Our findings show that the lowest score on the EORTC QLQ-C30 was the global health status, which tests for quality of life months to years after surgery. This measure was an overall quality of life measure but in prior studies, it was found that patients struggled most with social disability, handicap and psychological disability (21). We used the EORTC QLQ-C30 for quality of life measures and Yang et al used UW-QOL but both assessed similar measures(22). In our study, we found that constipation and insomnia were the two factors that patients continuously rated as being a problem so this may also contribute to their lowered quality of life. These symptoms are reported in the QLQ-C30, which lists global health status and not just related to head and neck or FFF reconstruction. Thus these can be attributed to natural aging process is a patient recovering from over all cancer treatment.

Both clinician and non-clinician ratings of the patients' esthetic appearance were lower than their early post operative pictures. This is secondary to atrophy of soft tissue and bone with passage of time, as well as long term deleterious effect of post operative radiotherapy leading to soft tissue atrophy and fibrosis. Finally, physicians rated patients' pictures much higher in both post-op and current photographs, which may be due to the fact that physicians have a more realistic view of post surgery appearances compared to non-clinicians who are simply rating patients' appearance with expectation of normal everyday appearance. We hypothesize that this may be due to physician's understanding of the impact of surgery versus non-clinicians whose expectations are different, due to a lack of understanding and acceptance of the detrimental effects of mandibulectomy and reconstruction with a FFF.

Interestingly, patients reported having a high physical function but physicians scored them to have just 64% of perfect function on the 11-item questionnaire. Absence of teeth and inadequate mastication are important factors, in addition to malocclusion in those with remaining teeth are primary factors leading to the lower scores. Oral competency is another factor contributing to this decline in the score. In a prior study, similar observations were reported showing that poor function in patients who had oral cancer was largely due to inability to wear dental prosthesis in non-radiated and radiated patients (23). Secondary placement of dental implants has not been met with much success, and only a few patients go on to complete implant placement and enjoy the benefits of implant supported stable dentures. The lower rating of patient satisfaction with oral function in our patients can be at least in part attributed to either no lower dentures or unsatisfactory removable dentures. In a study reported by Kumar et al using the EORTC QLQ c30, EORTC H&N 35 and OHIP14 to compare the quality of life and denture satisfaction outcomes in patients who had two or four implant-supported dental rehabilitation following segmental mandibulectomy and reconstruction with free fibula flap, they were able to show that implant supported dentures gave a better quality of life compared to removable dentures(21). The results were measured in 3-time points: before the surgery, 6-month post-surgery, and 1 year post-surgery. All patients had better functional outcomes when they were provided with implant supported dentures compared to conventional removable dentures. Thus, consideration should be given

to place immediate implants in FFFs at the time of reconstruction for implant supported more stable dentures. However, there are several constraints to such an approach. For example, the cost of immediate implants, which may not be covered by patient's insurance. In other situations some patients are simply not interested, or do not follow up, complete dental restoration with implant supported dentures.

There have been many cross-sectional as well as longitudinal studies of QoL issues following free flap reconstruction after maxillectomy/mandibulectomy (24,25,26,27). Bozec et al. reported on their series of all patients who underwent any free flap reconstruction of the head and neck from 2004 to 2005 who completed QoL-C30 and EORTC H&N35 before surgery, and at 6 and 12 months. Irradiated patients had poorer global QoL than non-irradiated patients (mean score 74.3%). This is probably due to the adverse consequences of radiotherapy on the head and neck area as attested by the higher level of head and neck symptoms in irradiated than in non-irradiated patients (33.3% and 21.4%, respectively). It may appear surprising that their patients reported a lower level of function and more head and neck symptoms at 1 year than at 6 months after surgery. From a clinical point of view, patients seem to improve their global health status and their functional outcomes as the interval from the treatment increases (24). However, with passage of time, long term effects of radiotherapy on progressive fibrosis and soft tissue and bone atrophy would account for lower level of function and more symptoms. In our study, there were no significant differences on any of the variables by radiotherapy status. For the PROs, surprisingly, patients who received radiotherapy, tended to have better function and fewer symptoms on the QLQ-C30, but they tended to have more symptoms than patients without radiotherapy on the QLQ-H&N35. However, the patients who did not receive radiotherapy tended to have their pictures rated more favorably than the radiated patients, but the differences were small and not statistically significant.

On the other hand, Korflage et al. caution that other factors, such as comorbidity, are far more important in determining the patients' QOL and this has to be considered when interpreting the results of the questionnaires regarding general health. (28) In their study, they observed a decrease in QoL to be caused by a small group of patients with severe comorbidity. Most of their patients with comorbidity were not irradiated. Thus, when comorbidity was accounted for in the specific head and neck module, the differences between the irradiated and non-irradiated patients even after 5 years, were felt to be related to the late effects of radiotherapy, such as xerostomia, trismus, and problems with swallowing and speech. Similarly, Terrell et al ranked comorbidity to be the second greatest predictor of decreased QoL in patients with head and neck cancer (29).

In a study by Posch et al. the esthetic outcome was scored more negatively by the independent investigator than patients. The investigator was always looking for a completely normal appearance rather than just an improvement related to the severity of the defect or condition. This is similar to the observations in our study, where the esthetic scores by non-clinicians were lower than that by clinicians. In the Posch study, objective evaluation of esthetics included color mismatch, flap contracture, and flap bulkiness to be mainly responsible for suboptimal esthetic appearance (30).

The observations of our study highlight several factors, which should be considered for future patients to improve their quality of life. Absence of lower teeth and malocclusion were some of the major factors impacting on oral function. Consideration should be given to address these issues with immediate dental implants in the FFF at the time of reconstructive surgery if technically and economically feasible.. In addition, innovative approaches to restore or recreate a more lasting temporomandibular joint to avoid mal occlusion should be addressed. The issue of xerostomia needs to be addressed with innovative techniques with radiotherapy such as intensity modulated proton therapy. In spite of these deficits a majority of patients in this study expressed a higher satisfaction score over all. However, implementation of correctable issues, will likely offer better quality of life to long term survivors after FFF reconstruction of the mandible.

This study has several deficiencies, which should be considered however in interpreting the observations reported here. Deterioration in esthetic appearance and function with the natural aging process has to be factored in,for all such studies. In addition each patient's perception and level of satisfaction / dissatisfaction is highly variable based on their expectations. Further,a much larger series of patients to study these issues is desirable, but is not likely to be feasible due to the progressive loss of life either to disease or unrelated causes. However, within these constraints, we feel that our study shades light on the long term esthetic and functional outcomes of patients undergoing FFF reconstruction of the mandible for oral cancer

Conclusion

A cohort of 25 long term survivors from oral cancer who underwent FFF reconstruction after mandibulectomy, were studied for functional and esthetic outcomes. Overall, physicians reported 64% functionality compared to normal. Patients reported overall a high level of functional score on QLQ-C30, but lower scores on H&N35. Esthetic scores were reported to be higher by clinicians than non-clinicians. Patients reported better smile scores than overall facial appearance. Although all domains of function and esthetic appearance in radiated patients were lower than in non-radiated patients, the differences were not statistically significant.

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Abbreviations:

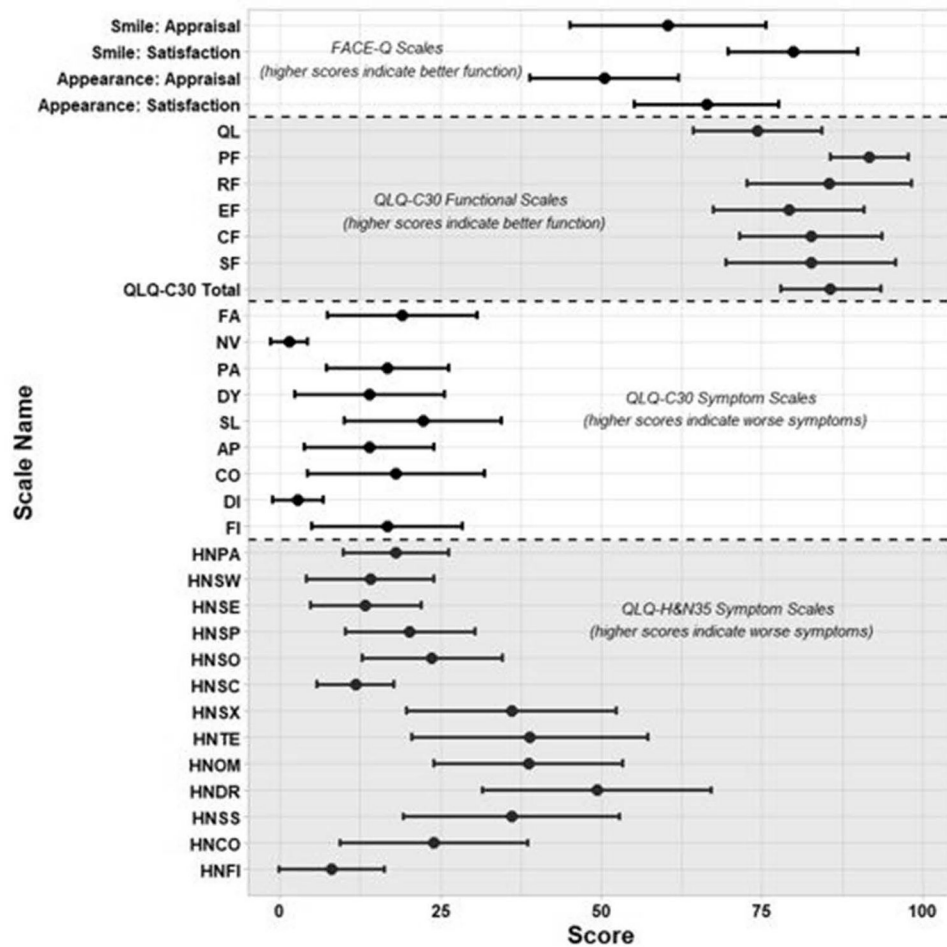
| | |
|--------------|--|
| FFF | fibula free flap |
| MSK | Memorial Sloan Kettering Cancer Center |
| EORTC | European Organization for Research and Treatment of Cancer |
| QLQ | quality of life questionnaire |
| CI | confidence interval |

| | |
|-------------|---------------------------|
| SCC | squamous cell carcinoma |
| QL | quality of life |
| PF | physical functioning |
| SL | insomnia |
| CO | constipation |
| NV | nausea/vomiting |
| HNTE | teeth |
| HNOM | opening mouth |
| HNSX | less sexuality |
| HNSS | sticky saliva |
| PRO | patient reported outcomes |

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**Figure 1.**

Means and 95% Confidence Intervals of Patient-Reported Outcome Measures.

Abbreviations: QL = Global health status/QoL; PF = Physical functioning; RF = Role functioning; EF = Emotional functioning; CF = Cognitive functioning; SF = Social functioning; FA = Fatigue; NV = Nausea and vomiting; PA = Pain; DY = Dyspnea; SL = Insomnia; AP = Appetite loss; CO = problems; HNSO = Trouble with social eating; HNSC = Trouble with social contact; HNSX = Less sexuality; HNTE = Teeth; HNOM = Opening mouth; HNDR = Dry mouth; HNSS = Sticky saliva; HNCO = Coughing; HNFI = Felt ill

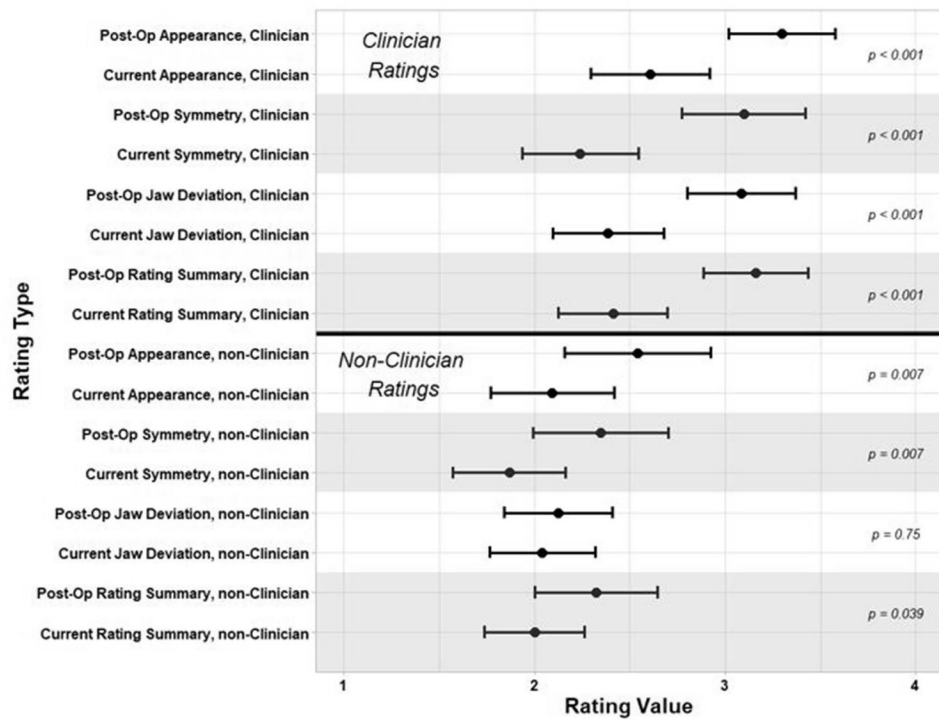


Figure 2.
Means and 95% Confidence Intervals of Clinician and Non-Clinician Esthetic Ratings of Post-Operative and Current Patient Photographs

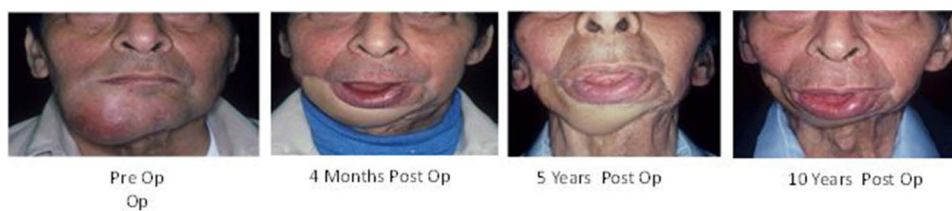


Figure 3.
An extreme example of progressive tissue atrophy



Figure 4.
Follow-up photographs in non-radiated patient

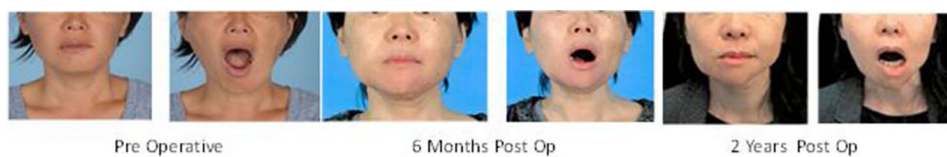


Figure 5.
Early post-radiation changes with atrophy and fibrosis



Figure 6.
Late post-radiation changes with atrophy and fibrosis

Table 1.

Comparison of outcomes by t-test and Wilcoxon p-values between radiated and not radiated patients

| PRO Variable | RTx ^a | | No RTx ^a | | t-test p-value |
|----------------------------|------------------|----------------------------|---------------------|----------------------------|----------------|
| | n ^b | Mean (95% CI) ^c | n ^b | Mean (95% CI) ^c | |
| Smile: Appraisal | 10 | 58.2 (42.9, 73.6) | 4 | 65.8 (2.7, 128.8) | 0.74 |
| Smile: Satisfaction | 16 | 83.8 (74.1, 93.4) | 5 | 67.2 (28.3, 106.1) | 0.31 |
| Appearance: Appraisal | 16 | 51.4 (37.1, 65.7) | 4 | 46.5 (21, 72) | 0.65 |
| Appearance: Satisfaction | 18 | 65.4 (52.8, 78.1) | 6 | 69 (34.3, 103.7) | 0.82 |
| QL ^d | 18 | 75 (65.1, 84.9) | 6 | 72.2 (35.7, 108.8) | 0.86 |
| PF ^e | 18 | 93.3 (87.3, 99.4) | 6 | 86.7 (65, 108.3) | 0.48 |
| RF ^f | 18 | 88 (74.4, 101.5) | 6 | 77.8 (35.4, 120.1) | 0.58 |
| EF ^g | 18 | 82.4 (70.4, 94.5) | 6 | 69.4 (30.1, 108.8) | 0.46 |
| CF ^h | 18 | 86.1 (74.7, 97.6) | 6 | 72.2 (36.1, 108.4) | 0.39 |
| SF ⁱ | 18 | 86.1 (73, 99.2) | 6 | 72.2 (25.7, 118.7) | 0.49 |
| FA ^j | 18 | 16 (3.6, 28.5) | 6 | 27.8 (-9.6, 65.2) | 0.48 |
| NV ^k | 18 | 0 (0, 0) | 6 | 5.6 (-8.7, 19.8) | 0.36 |
| PA ^l | 18 | 15.7 (6.5, 24.9) | 6 | 19.4 (-16.3, 55.1) | 0.81 |
| DY ^m | 18 | 11.1 (-1.6, 23.8) | 6 | 22.2 (-13.9, 58.4) | 0.49 |
| SL ⁿ | 18 | 18.5 (5.5, 31.5) | 6 | 33.3 (-5, 71.7) | 0.39 |
| AP ^o | 18 | 11.1 (3.1, 19.2) | 6 | 22.2 (-20.1, 64.6) | 0.54 |
| CO ^p | 18 | 13 (-1.1, 27.1) | 6 | 33.3 (-10.9, 77.6) | 0.31 |
| DI ^q | 18 | 1.9 (-2.1, 5.8) | 6 | 5.6 (-8.7, 19.8) | 0.55 |
| FI ^r | 18 | 14.8 (0.6, 29) | 6 | 22.2 (-6.3, 50.8) | 0.58 |
| QLQ-C30 ^s Total | 18 | 88.4 (81.9, 94.8) | 6 | 77.6 (46.5, 108.7) | 0.42 |
| HNPA ^t | 19 | 16.7 (7.5, 25.8) | 6 | 22.2 (-2.9, 47.4) | 0.62 |
| HNSW ^u | 19 | 16.7 (3.8, 29.6) | 6 | 5.6 (-3.5, 14.6) | 0.13 |
| HNSE ^v | 19 | 13.2 (3.7, 22.7) | 6 | 13.9 (-14.1, 41.9) | 0.95 |
| HNSP ^w | 19 | 21.9 (8.9, 34.9) | 6 | 14.8 (0.7, 28.9) | 0.40 |
| HNSO ^x | 19 | 23.7 (9.3, 38.1) | 6 | 23.6 (10.7, 36.5) | 0.99 |
| HNSC ^y | 19 | 12.6 (5.2, 20) | 6 | 8.9 (-4.1, 21.9) | 0.56 |
| HNSX ^z | 19 | 40.4 (19.9, 60.8) | 6 | 22.2 (-6.3, 50.8) | 0.24 |
| HNTE ^{aa} | 18 | 46.3 (23.5, 69.1) | 6 | 16.7 (-12.6, 45.9) | 0.08 |
| HNOM ^{ab} | 19 | 43.9 (26.1, 61.7) | 6 | 22.2 (-6.3, 50.8) | 0.15 |
| HNDR ^{ac} | 19 | 52.6 (32.4, 72.9) | 6 | 38.9 (-12.6, 90.4) | 0.56 |

| PRO Variable | RTx ^a | | No RTx ^a | | t-test p-value |
|--------------------|------------------|-----------------------------|---------------------|-----------------------------|----------------|
| | n ^b | Mean (95% CI ^c) | n ^b | Mean (95% CI ^c) | |
| HNSS ^{ad} | 19 | 38.6 (19.1, 58.1) | 6 | 27.8 (-18.7, 74.3) | 0.61 |
| HNCO ^{ae} | 19 | 21.1 (3.9, 38.2) | 6 | 33.3 (-5, 71.7) | 0.49 |
| HNFI ^{af} | 19 | 8.8 (-1.7, 19.3) | 6 | 5.6 (-8.7, 19.8) | 0.67 |

^a-RTx- radiotherapy;

^b- n- number;

^c- CI- confidence interval;

^d- QL- quality of life;

^e- PF- physical functioning;

^f- RF- role functioning;

^g- EF- emotional functioning;

^h- CF- confidence functioning;

ⁱ- SF- social functioning;

^j- FA- fatigue;

^k- NV- nausea/vomiting;

^l- PA- pain;

^m- DS- dyspnea;

ⁿ- SL- insomnia;

^o- AP- appetite loss;

^p- CO- constipation;

^q- DI- diarrhea;

^r- FI- financial difficulties;

^s- QLQ-C30- quality of life questionnaire C30;

^t- HNPA- pain;

^u- HNSW- swallowing;

^v- HNSE- senses problems;

^w- HNRP- speech problems;

^x- HNSO- trouble with social eating;

^y- HNCS- trouble with social contact;

^z- HNSX- less sexuality;

^{aa}- HNTE- teeth;

ab-HNOM- opening mouth;

ac-HNDR- dry mouth;

ad-HNSS- sticky saliva;

ae-HNCO- coughing;

af-HNFI- felt ill.

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