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ORIGINAL ARTICLE

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Dental implant-based oral rehabilitation in patients reconstructed with free fibula flaps: Clinical study with a follow-up 3 to 6 years

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Abstract

Background: Oral rehabilitation of patients after maxillofacial reconstructive surgery represents a challenge and stable prosthetic retention can be achieved with the use of dental implants.

Purpose: This retrospective report aimed to evaluate implant-based oral rehabilitation following maxillofacial reconstruction with free fibula flaps.

Materials and Methods: A total of 14 patients who had reconstruction with fibula flaps either by CAD/CAM or conventional surgery were included in this study. A total of 56 implants (40 in flaps, 16 in native bone) were evaluated. Follow-up after reconstructive surgery ranged between 3.25 and 6.3 years. Follow-up after implant surgery ranged between 1.5 and 3.8 years.

Results: Overall survival rate was 85.7% in free fibula flaps and 85.6% in dental implants. Eight implants were lost in three patients and all of these failures were in dental implants inserted in free flaps. According to the results on patient basis, the implant survival was not influenced by any variable.

Conclusions: The maxillofacial reconstruction with free fibula flap and oral rehabilitation with implant-supported prostheses after ablative surgery can be considered as an effective and safe procedure with successful aesthetic and functional outcomes.

KEYWORDS

dental implants, free fibula flap, jaw reconstruction, maxillofacial reconstructive surgery, oral rehabilitation

1 | INTRODUCTION

The reconstruction of the segmental oral defects may be required following trauma, infection, tumor resection, or osteoradionecrosis and to repair congenital deformities.[1,2] Maxillofacial region represents a special challenge due to the functional and anatomical complexity. Additionally, the mandible morphologically frames the lower third of the face, which is important in terms of esthetics.[1] A reconstruction with vascular free flaps and rehabilitation with fixed dental prothesis with the use of dental implants can offer patients optimum results as esthetics, nutrition, and speech.[1,3]

Since its introduction by Hidalgo,[4] free fibula flap (FFF) is considered as the gold standard for maxillofacial reconstruction after ablative surgery among other free flap options, such as anterolateral thigh and the radial forearm flap.[1,2,5-7] The fibula has multiple advantages, including bone length and thickness, low donor site morbidity, and

donor site location permitting flap harvest simultaneously with tumor resection in two team approach.[5,8]

A drawback of fibula for mandibular reconstruction is its limited height. Fibula is best positioned at the inferior border of the mandible to reproduce contours of the lower third of the face, which can lead to an intra-oral height discrepancy with the native mandible and occlusal plane.[7] In order to overcome height discrepancy, one solution is to place fibula more superiorly, around 10 to 15 mm inferior to the occlusal plane, to provide sufficient bone height for placement of implants.[9] The inferior border may be reconstructed with a supplementary 2.4-mm reconstruction plate to restore lower facial projection. Another solution is "double-barrel technique," in which, fibula is folded in order to increase bone height and to minimize the discrepancy between the occlusal plane and reconstruction.[10,11] Vertical distraction osteogenesis, using a horizontal osteotomy, can also be applied secondarily to gain adequate alveolar height.[12] In FFF surgery, preoperative angiogram is recommended due to its high positive predictive value and sensitivity in detecting vascular aberrations, especially for the patients with known peripheral vascular disease, previous leg trauma, or previous leg surgery.[7,13]

Currently, the evolution of computer-aided design/computer-aided manufacturing (CAD/CAM) technologies has introduced three-dimensional (3D) approaches to virtual surgical planning by preparation of 3D models for vascular free grafts prior to surgery.[14]

Stereolithographic models of the resection site in mandible/maxilla and the donor fibular bone site can be obtained from computer tomography scan data before the surgery.[14]

Surgical plates can be prepared preoperatively, according to the 3D data obtained from the CBCT of the patient in order to increase the accuracy and decrease the duration of surgery. Each step of the operation including the osteotomies on the mandible and the fibula can be preplanned by use of staged cutting guides.[15] Currently, preoperative virtual surgical planning (VSP) is a widely accepted concept to improve the results of the surgical reconstruction procedures in the maxillofacial region.[16-18]

In most cases, the reconstruction of the maxillofacial defect is not enough for the restoration of oral function in patients.[19] Currently, dental rehabilitation with dental implants and prosthesis is considered as a successful treatment modality for the restoration of physiological functions and esthetics, and for increasing the quality of life of such individuals.[3,12,20-24]

The aim of this retrospective clinical report was to evaluate the clinical outcomes of dental implant-based oral rehabilitation in patients that underwent ablative surgery and maxillofacial reconstruction with free fibula flaps.

2 | MATERIALS AND METHODS

In this retrospective report, clinical outcomes of oral rehabilitation with dental implants in patients who had reconstructive surgery with free fibula flaps were assessed. The study population composed of 14 patients that underwent maxillofacial reconstruction surgery between November 19, 2013 and December 13, 2019 and implant insertion between May 5, 2016 and September 13, 2018. All the patients were treated at the Department of Oral Science and Maxillofacial surgery, University of Milan. A signed informed consent form was obtained from all subjects for the treatment protocol. This study was in compliance with the principles laid down in the Declaration of Helsinki on medical protocol and ethics and the study protocol was approved by the Ethics Committee of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Regione Lombardia with date February 21, 2017 Ethics Committee of Milano Area B Act 478/2017.

The inclusion criterion was patients who had oral rehabilitation with dental implants after ablative surgery and reconstructive surgery with free fibular flaps. No exclusion criterion was set.

2.1 | Presurgical protocol

A standard protocol was applied to all patients prior to maxillofacial surgery. The patients were examined by preoperative cone beam computed tomography (CBCT) scans for the lesion evaluation. General health status of the patients was checked by electrocardiography, chest radiography and a blood test. Preoperative angiogram from the leg was also obtained to detect vascular aberrations. The patients were prescribed with pre- and post-operative antibiotics: Augmentin (amoxicillin and clavulanate potassium) at a dosage of 1-g tablet or Azithromycin 500 mg as an alternative in cases of allergy to penicillin. In patients that had CAD/CAM guided surgery, the resection and the resconstruction of the lesions with microvascularized FFFs were planned and performed with the use of Materialize ProPlan CMF (Materialise, Technologielaan 15, 3001 Leuven, Belgium).

2.2 | Preoperative CAD/CAM protocol

Preoperative planning of the patients was done by processing DICOM (Digital Imaging and Communications in Medicine) files of both mandible and fibula by ProPlan CMF software (Materialise, Technologielaan 15, 3001 Leuven, Belgium) via web-based PROPLAN CMF service with the support of medical engineer at Materialise headquarter in Belgium. Resection of the lesion and segmentation of free fibular flap were simulated on the 3D virtual models (SLT files). Vertical height of native bone site was matched with that of new bone (segmented fibula). After the final validation, the patient-specific maxilla/mandibula and fibular surgical cutting guides with SLT model and custom made specific reconstructive plate were created approximately within 10 working days.

2.3 | Surgical protocol

Under general anesthesia and after tracheotomy, operation started simultaneously by two teams. In CAD/CAM cases, the following standard protocol was applied: first team excised the tumor via intraoral

approach with the aid of cutting guide and prepared recipient neck vessels for microanastomosis through neck incision, while second team harvested free fibula flap with the aid of fibula cutting and reconstruction guide. In cases that underwent conventional surgery, the same protocol was applied without any guides for resection and reconstruction. Finally, in all patients, free fibula flap (either single barrel, double barrel or fibula flap with osteodistraction) was fixed to defect site with reconstructive titanium plate and screws (osteosynthesis material) and microvascular anastomosis was done. Both donor and recipient site wounds were closed primarily with insertion of suction drain in the lower limb and soft drain in the neck for 48 hours. Leg split was inserted for 1 week to ensure ankle stability in early postoperative period. Patient was referred to intense care unit in the first postoperative day then was admitted to ward where he was weaned from tracheotomy after 48 hours. All the patients discharged of the hospitalization approximately after 10 days with strict follow up of donor and recipient sites.

Second stage surgery for oral rehabilitation was the implant insertion that was performed under local anesthesia (4% articaine with 1:100 000 adrenalin). In brief, the surgical protocol applied for implant surgery is described below. The operation started with crestal incision with vertical releasing incisions and full thickness flap reflections. All the bone surgeries and the implant site preparations were performed using drills and burs according to the instructions from the manufacture firms. Finally, the implants were carefully inserted at a low speed, with a torque of 40 to 80 Ncm, and the final stabilization was controlled manually with an extraoral screwdriver. The length of the implant was determined to have bicortical anchorage to achieve primary stability. During the implant surgery, the titanium reconstructive plates and screws were totally or partially removed in cases where they interfered with the appropriate placement of dental implants.

Mean interval period between two surgeries was 24.6 months (0 to 3.5 years). Three different implant brands were used in this work: In 10 patients Biomet 3i Implants (Florida, US), in 2 patients Intra-Lock implant (Birmingham, US), and in 2 patients Megagen Implant (Merone, Italy). In just one of the patients, dental implants were inserted simultaneously at the time of the reconstructive surgery.

The same follow-up protocol was applied after reconstructive and dental implant placement surgeries. The follow-up protocol with clinical and radiographic examinations was set as 1 month, 3 months, 6 months, and 12 months then every 6 months for the following years. Figure 1 shows panoramic radiograph of a patient with two dental implants inserted in free fibular flap and two dental implants inserted in native bone.

All of the patients were referred to oral hygienists, before implant surgeries, in order to maintain oral health and care. Routine follow up of the patients by the oral hygienists continued until they received their final prostheses. The implants were uncovered in a timing mostly dependent on the patient specific factors, such as general and oral health status of the patient. All the patients received temporary prosthesis within 1 or 2 weeks. The decision for type of prosthesis and timing of the delivery of the final prosthesis based on the economic, oral and general health condition of the patient.

2.4 | Evaluation of success

Implant survival was the taken as primary outcome of the study and was evaluated at each appointment according to the clinical parameters which are listed below.

- absence of pain, and infections at implant site;
- absence of implant mobility and peri-implant radiolucency;
- no implant failure due to revision surgery or flap failure;
- no spontaneous implant failure.

Postoperative complications of fibula flaps and dental implants and complications at prosthetic phase were evaluated in detail for each case.

2.5 | Statistical analysis

Statistical analysis was performed using GraphPad Prism 5.03 (GraphPad Software, Inc., La Jolla, California). Descriptive statistics of

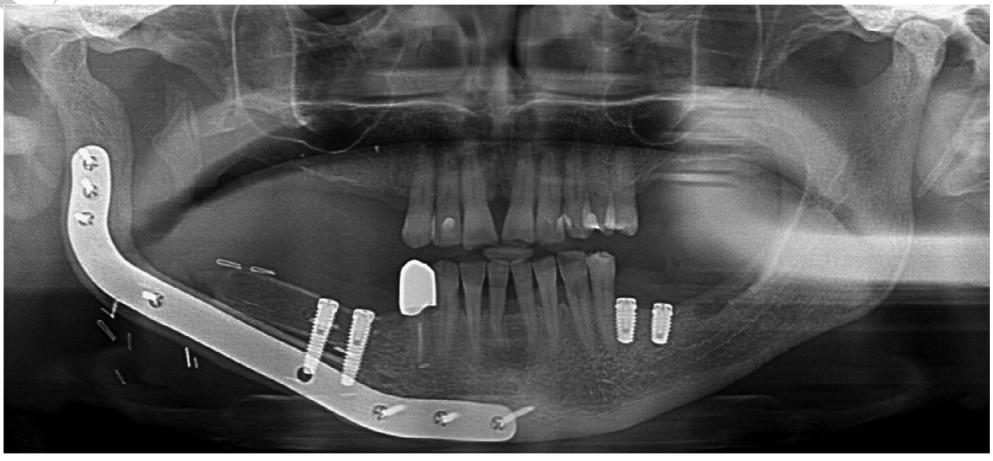

FIGURE 1 Panoramic radiograph of a patient with two dental implants inserted in free fibular flap and two dental implants inserted in native bone

the data was done using mean values and SD for quantitative variables normally distributed. Normality of distributions was evaluated through the d'Agostino and Pearson omnibus test. The effect of each variables (gender, age (more than 65), reason for maxillofacial surgery, reconstruction site, type of surgery (conventional vs CAD/CAM), timing of implant insertion, implant location, fibular flap type, site, radiotherapy, chemotherapy, type of prosthesis) on implant survival was evaluated by using the Fisher's exact test given the low incidence of complications in each subgroup. When there were more than two categories for a given variable, the generalized Fisher exact test was used. Since the latter was not provided by GraphPad Prism 5.03, the test was performed using the online free package SISA (Simple Interactive Statistical Analysis, http://www.quantitativeskills.com/sisa/). The distribution of failure of implants was assessed using a time-to-event analysis. Cumulative survival rate was estimated through Kaplan-Meier analysis. The cumulative incidence of failures of implants placed in native bone and in flaps was compared using log-rank (Mantel-Cox) test. Patient was the primary unit of analysis. However, implant as unit of analysis was also considered. $P = .05$ was considered as the significance threshold.

This article was written following the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (http://www.strobe-statement.org).

3 | RESULTS

A total of 14 patients (6 male-8 female) with a mean age of 52.14, SD 17.7 years (range 21-79 years) were included. Fifty-six dental implants were placed (40 implants in FFF and 16 implants in native bone) for oral rehabilitation of the patients. There were no dropouts. All of the 14 patients had implants in inserted in FFF. Nine patients had implants inserted only in FFF, and five patients had additional implants inserted in native bone. The mean follow-up after FFF surgery was 54.41 ± 12.22 (range 39-76) months. The mean follow-up after implant surgery was 31.78 ± 7.94 (range 18-46) months. The mean interval period between two surgeries was 24.6 months (0-44 months).

Cumulative dental implant survival rate was 85.6% (79.75% for implants in flaps, 100% in native bone) as can be seen in Figure 2. FFF survival rate was 85.7%. Different patient characteristics such as; age, gender, reason for ablative surgery, surgery site, fibula flap type, type of prosthesis, implant location and timing were evaluated. The data concerning implant survival are listed in Table 1. According to the results on patient basis, the implant survival was not influenced by any variable (Table 1). Reason for maxillofacial surgery (disease type) was not assessed due to large diversity with low incidences among the variables.

According to the results of analysis on implant basis, implant survival was not influenced by the type of surgery (CAD/CAM vs Conventional surgery), and type of free fibular flap. Males, maxillary site, and simultaneous implant insertion at the time of maxillofacial surgery showed significant failures on implant basis. However, it can be stated that one male patient who had simultaneous implant insertion at maxillary site hampered the result. In fact, this patient experienced a cluster of six implant failures and graft failure 2 weeks after surgery. Implant insertion in native bone was found to be particularly favorable in terms of implant survival. However the difference in cumulative implant survival rate between implants placed in native bone and flap, evaluated by means of the Log-rank (Mantel-Cox) test, did not achieve significance ($P = .054$, Figure 2).

Three patients had Toronto and five patients had fixed bridge prosthesis. Six patients have temporary prosthesis. One patient had the final Toronto prosthesis delivered at the same day of the implant insertion. For the other patients, the implants were uncovered at least 3 months after implant insertion surgery, mostly depending on various patient specific factors. When conducting the analysis for prosthesis type, temporary prosthesis was found to have more impact on failures. However, as mentioned previously, when conducting the analysis on patient basis, no significant effect of any considered factors on implant failure was found (Table 1).

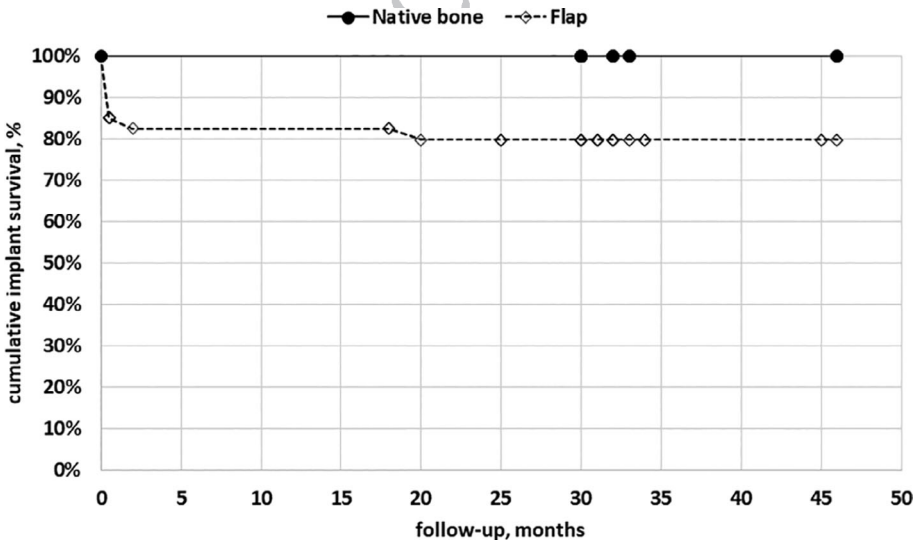

FIGURE 2 Cumulative implant survival rate with Kaplan-Meier analysis

TABLE 1 Patient characteristics and implant survival

Patient	Characteristics	Patients with failures/total no. of patients	Survival %	*P*-value (patient based)	Failed implants/ total no. of implants	Survival %	*P*-value (implant based)
Sex	Male	2/6	66.6	.33	7/17	76.5	<.001*
	Female	1/8	87.5		1/39	97.4	
Reason for maxillofacial surgery	MEC	No fail/1	100	N/A	No fail/4	100	N/A
	SCC	1/6	83.3		1/30	96.7	
	Fusocellular phleomorfic neoplasia	No fail/1	100		No fail/3	100	
	Chronica sclerosing osteomyelitis	No fail/1	100		No fail/3	100	
	Keratocystic	2/2	0		7/8	12.7	
	Odontogenic mixoma	No fail/1	100		No fail/3	100	
	Ossifying fibroma	No fail/1	100		No fail/2	100	
	Gorlin Gortz	No fail/1	100		No fail/3	100	
Maxillofacial reconstruction site	Mandible	2/13	84.6	.34	2/50	96.0	<.001*
	Maxilla	1/1	0		6/6	0	
Flap type	Single barrel	2/9	77.8	1.00	7/38	94.9	.64
	Double barrel	1/4	75.0		1 /15	91.7	
	Distraction osteogenesis and FFF	0/1	100		0 /3	100	
Radiotherapy	Yes	0/2	100		0/6	100	.38
	No	3/12	66.7		8/50	84	
Chemotherapy	None	—	—		—	—	N/A
Type of prosthesis	Toronto	0/3	100	.75	0/21	100	.001*
	Bridge	1/5	80.0		1/16	93.8	
	Temporary	2/6	56.7		7/19	63.2	
Smoking habits	None	—	—		—	—	N/A
Age	>65	1/3	66.7	.45	1/13	92.3	.29
	<65	2/11	81.8		7/43	83.7	
Type of surgery	CAD/CAM	2/6	66.7	.33	7/34	79.4	.08
	Conventional	1/8	87.5		1/22	95.4	
MX location	Anterior	2/3 (1Mx/2Md)	33.3	.12	7/11	36.3	<.001*
	Posterior	1/9	88.9		1/45	97.8	
Implant insertion	Simultaneous	1/1	0	.34	6/6	0	<.001*
	Delayed	2/13	84.6		2/50	96.0	
Implant location	Native bone	0/5	100	.23	0/16	100	.054
	Flap	3/9	66.7		8/40	79.8	
Total		3/14	78.6	N/A	8/56	85.7	N/A

*P = .05 as statistically significant difference; Mx, maxilla; Md, mandible; N/A, not applicable; FFF, free fibular flap.

In the population, none of the patients received chemotherapy and there were no smokers (there were 4 ex-smokers, but they did not have failure). Two of the patients received radiotherapy (66GY T; 56Gy N). However, in one of the patients, radiotherapy was interrupted due to a mucositis lesion and was not continued afterwards.

Failures following free fibula flap reconstructive and implant placement surgeries are listed in Table 2.

Additional soft tissue corrections were done in two patients with free palatal soft tissue grafts, in order to augment peri-implant soft-tissue volume.

TABLE 2 Fibula flap and implant failures in five patients

Implant failures
• Six implant failures: Six implants failed in the patient who had simultaneous six implant insertion at the time of resective and reconstructive surgery. Fifteen days after first surgery, due to failure of FFF, all of the six implants were removed at a second resective and reconstructive FFF surgery without any insertion of implants. However, the second FFF also failed after 18 months and the patient received zygomatic implants after additional 6 months.
• One implant failure: one fistula around implants. One implant and osteosynthesis plate was removed at a revision surgery after 32 months. This patient still has a temporary bridge.
• One implant failure: Implant removal and second resective and reconstructive surgery due to SCC recurrence 29 months after maxillofacial reconstructive surgery.
Flap failures
• Failure in single barrel FFF after 2 weeks (six implants lost due to flap failure). The patient had a second FFF reconstructive surgery which also failed after 18 months. Treatment: The patient received four zygomatic implants with CAD/CAM guided surgery.
• Failure in FFF with osteodistraction: Cutaneous fistula during distraction. Treatment: Fistulectomy and distractor removal (this patient had three implants and none of them were removed). Prosthesis is still at temporary phase.

One of the patients had oral mucositis and another patient had hyperkeratosis lesion (confirmed with biopsy). As a treatment for these patients, the prostheses were removed and healing abutments were repositioned. They were additionally recalled for additional oral hygiene sessions and controls.

Complications that were seen at any stage and treatment modalities applied are listed in Table 3.

TABLE 3 Complications/events and treatment methods in eight patients

Complication/event	Treatment
SCC recurrence in two patients (one tumor recurrence happened at 29 months and one implant was removed. The other SCC recurrence happened at 62 months)	Revision surgeries
Cutaneous fistula during osteodistraction	Revision surgery for fistulectomy and distractor removal at 45 months after first surgery
Painful neuropathy of the lower face third (left mandible) at 11 months after surgery	Frequent controls and medications for pain
Oral bleeding from wound dehisce at the inferior right fornix	Superficial temporal artery clip under general anesthesia (1 month after surgery)
Mandibular condyle dislocation and cutaneous fistula	Surgical revision and condyle necrotic part removal (1 month after surgery).
Hyperkeratosis	Adjustments of the temporary prosthesis and more frequent control appointments (at 62 months)
In Gorlin-Golz syndrome patient that had FFF in mandible, keratocystic odontogenic tumor recurrence at both maxilla and mandibula	Tumor removal followed by Le-fort 1 maxillectomy and major reconstructive surgery due to malocclusion
Oral mucositis	Adjustments in temporary prosthesis and repositioning of healing abutment (at 39 months)

4 | DISCUSSION

The use of autologous microvascular free fibula flaps in management of the maxillofacial reconstruction is associated with advantages such as; the low donor-site morbidity and the availability of tissues allowing the closure of the defect.[5,11,20,25,26] Additionally, in FFF harvesting, there is no need to change the position of the patient during operation, which makes it a better option when choosing between scapula flap or FFF.[5,25] However, although fibula offers several advantages over scapula, radius and ilium,[25] it cannot be said that it is the most successful, because each patient's health condition and defect site is unique and decision should be always patient specific.

The results that are reported in literature for comparison of functional outcomes of patients who received a FFF for the reconstruction of a maxillofacial defect is generally hampered by diversity in the bone and soft tissue defects.[20,27] Symphysis area has a profound effect on function than lateral mandibular defects and large defects requiring multisegment reconstructions cause more loss of function compared to small sized defects with single segment FFF.[20,27-29] One of the main limitations of FFF is the height discrepancy with the mandible, which can be overcome by techniques such as, double-barrel.[21,30]

Although FFFs are considered as successful, in clinical applications ideal function and esthetic goals are not achieved yet.[11] Utilizing computer-aided design/computer-aided manufacturing (CAD/CAM) technologies might offer many advantages since virtual presurgical planning and cutting guides can improve the results of surgical reconstruction in terms of time and successful results.[31] Excellent precision can be achieved with custom cutting guides for osteotomies of the fibula and mandible. Shaping session is easier due to no guesswork and duration of ischemia dramatically decreases.[32-35] Disadvantages of these systems are the high cost, and the need for a professional software tool, which limit their wide use.[32] However, an article by Bolzoni et al[16] discussed the cost analyses, comparing CAD/CAM guided surgery to conventional surgery. As a result, they reported that CAD-CAM technology has a comparable expense to the conventional freehand technique, specifically for defects requiring at least 3 fibular segments. In accordance with literature, the preoperative expenses were higher in CAD/CAM patients. However, postoperative stay and operative theater occupation were shorter in the CAD-CAM group vs the conventional group, which consequently decreased the postoperative costs.[16]

In this study, FFF was not compared to other types of flaps and the decision mostly was dependent on the defect site and size. According to the results, FFF survival was 85.7% and FFF failure happened in two patients. One of the failures was seen in single barrel FFF 2 weeks after the operation. This patient received a second FFF reconstruction, however this secondary flap also failed. The treatment modality was totally changed and quad zygoma implants were inserted as an alternative solution. Another patient had cutaneous fistula during osteodistraction with FFF. This patient was treated with fistulectomy and the distractor was removed.

The oral rehabilitation after ablative surgery is quite demanding and following surgical reconstruction, patients usually suffer from functional disabilities and esthetic deformity.[36] The use of prostheses with dental implants can be beneficial as confirmed by various reports.[3,8,20,23,24] According to the results of this report, overall survival rate was 78.6% for dental implants which is in accordance with the literature showing promising results.

In this study, eight implants were lost in three patients and all of these failures were in dental implants inserted in free flaps. One of the patients lost six implants due to failure in FFF. The other implant failure was because of a SCC recurrence and the implant was removed during a revision surgery. The third patient lost an implant due to fistula. The first patient with failures had simultaneous implantation at the time of the surgery and lost all of the six implants. The two of the failures were seen in CAD/CAM guided surgery. However, it cannot be said that "immediate implantation at the time of the reconstructive maxillofacial surgery" or "CAD/CAM surgery" can be associated with higher risk of failure. In this study, males, maxilla (as implant insertion and maxillofacial site) and simultaneous implant insertion at the time of maxillofacial surgery showed more failures. However, this was not statistically significant on patient basis and one male patient who experienced six early implant failures at maxillary site, after receiving implant placement with CAD/CAM guided surgery, simultaneously to flap procedure, majorly influenced such result. Additionally, there are several recent reports in literature with successful results on "simultaneous implantation"[22-24] and on "CAD/CAM guided surgery."[17,37-39]

Although the concept of virtual surgical planning simplifies significantly the mandibular reconstruction with microvascular free flaps, further improvement of resection and reconstruction accuracy are still necessary for optimum results. Data regarding the accuracy of this concept are scarce and the surgical models are expensive.[11,18,40] However, currently there is an increasing number of publications reporting promising results.[17,40,41] Another future direction is to use navigation guided surgery. Navigated resection and modeling of the flaps is considered as the next step in the evolution of computer-assisted reconstruction of mandibular defects with possible more safe and accurate results.[42,43]

The location of dental implant placement (mandible or maxilla) on implant failure was evaluated in literature with conflicting results. Schoen et al,[44] reported more failures in the maxilla while Pompa et al,[19] found no difference among arches. In this study, only one patient had six implants placed in maxillary bone and lost all of them. So, no conclusions can be drawn regarding a difference in implant failure between arches in the present study.

There is no consensus in literature for optimum dental prosthesis type among reports, which is probably because of the large individual variability regarding the location and dimension of the maxillofacial defects. According to the results of this study, temporary prosthesis was found to have some impact on failures on implant basis. However, this was due to the postponed delivery of the final prosthesis when patients had major or minor complications. So, it cannot be concluded that temporary prosthesis is less successful.

Implant survival can be influenced by several reasons such as health status, disease type, radiotherapy, oral hygiene, soft tissue, implant height, and width.[19,45] The retrospective design of this study can be considered as one of the limitations. There is an increasing interest in literature for oral rehabilitation with dental implants in maxillofacial patients with large defects; however, currently there is still a limited number of reports evaluating this type of treatment modality with long follow up periods.

5 | CONCLUSIONS

According to the results of this present study, the reconstruction with free fibula flap and oral rehabilitation with implant-based prostheses after resection surgery in patients with large defects can be considered as an effective and safe procedure with promising successful aesthetic and functional outcomes.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

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REFERENCES

1. Takushima A, Harii K, Asato H, Momosawa A, Okazaki M, Nakatsuka T. Choice of osseous and osteocutaneous flaps for mandibular reconstruction. *Int J Clin Oncol*. 2005;10:234-242. https://doi.org/10.1007/s10147-005-0504-y.
2. Kesting MR, Hölzle F, Wales C, et al. Microsurgical reconstruction of the oral cavity with free flaps from the anterolateral thigh and the radial forearm: a comparison of perioperative data from 161 cases. *Ann Surg Oncol*. 2011;18:1988-1994. https://doi.org/10.1245/s10434-011-1584-8.
3. Pellegrino G, Tarsitano A, Ferri A, Corinaldesi G, Bianchi A, Marchetti C. Long-term results of osseointegrated implant-based dental rehabilitation in oncology patients reconstructed with a fibula free flap. *Clin Implant Dent Relat Res*. 2018;20:852-859. https://doi.org/10.1111/cid.12658.

4. Hidalgo DA. Fibula free flap: a new method of mandible reconstruction. *Plast Reconstr Surg*. 1989;84(1):71-79.
5. Ward BB, Kang DR. Reconstructive surgery: fibula. In: Kademani D, Tiwani P, eds. *Atlas of Oral & Maxillofacial Surgery*. 1st ed. Missouri: Elsevier; 2016:1197-1211.
6. Wei FC, Seah CS, Tsai YC, Liu SJ, Tsai MS. Fibula osteoseptocutaneous flap for reconstruction of composite mandibular defects. *Plast Reconstr Surg*. 1994;93:294-304. discussion 305-306.
7. Chim H, Saldago CJ, Mardini S, Chen H-C. Advances in head and neck reconstruction, part I. IN: reconstruction of mandibular defects. *Semin Plast Surg*. 2010;24(2):188-197. https://doi.org/10.1055/s-0030-1255336.
8. Awad ME, Altman A, Elrefai R, Shipman P, Looney S, Elsalanty M. The use of vascularized fibula flap in mandibular reconstruction. A comprehensive systematic review and meta-analysis of the observational studies. *J Craniomaxillofac Surg*. 2019;47:629-641. https://doi.org/10.1016/j.jcms.2019.01.037.
9. Wallace CG, Chang YM, Tsai CY, Wei FC. Harnessing the potential of the free fibula osteoseptocutaneous flap in mandible reconstruction. *Plast Reconstr Surg*. 2010;125:305-314.
10. Bahr W, Stoll P, Wachter R. Use of the "double barrel" free vascularized fibula in mandibular reconstruction. *J Oral Maxillofac Surg*. 1998;56:38-44.
11. Kokosis G, Schmitz R, Powers DB, Erdmann D. Mandibular reconstruction using the free vascularized fibula graft: an overview of different modifications. *Arch Plast Surg*. 2016;43:3-9.
12. Iizuka T, Hallermann W, Seto I, Smolka W, Smolka K, Bosshardt DD. Bi-directional distraction osteogenesis of the alveolar bone using an extraosseous device. *Clin Oral Implants Res*. 2005;16:700-707. https://doi.org/10.1111/j.1600-0501.2005.01185.x.
13. Fukaya E, Grossman RF, Saloner D, Leon P, Nozaki M, Mathes SJ. Magnetic resonance angiography for free fibula flap transfer. *J Reconstr Microsurg*. 2007;23:205-211.
14. Yeung RW, Samman N, Cheung LK, et al. Stereomodel-assisted fibula flap harvest and mandibular reconstruction. *J Oral Maxillofac Surg*. 2007;65:1128-1134.
15. Hirsch DL, Garfein ES, Christensen AM, Weimer KA, Saddeh PB, Levine JP. Use of computer-aided design and computer-aided manufacturing to produce orthognathically ideal surgical outcomes: a paradigm shift in head and neck reconstruction. *J Oral Maxillofac Surg*. 2009;67:2115-2122.
16. Bolzoni AR, Segna E, Beltramini GA, Sweed AH, Gianni AB, Baj A. Computer-aided design and computer-aided manufacturing versus conventional free fibula flap reconstruction in benign mandibular lesions: an Italian cost analysis. *J Oral Maxillofac Surg*. 2019;78:1035.e1-1035.e6. https://doi.org/10.1016/j.joms.2019.03.003.
17. Ferri A, Varazzani A, Bolzoni AR, et al. A multicenter survey on computer-aided design and computer-aided manufacturing mandibular reconstruction from Italian community. *Microsurgery*. 2019;39:673-674. https://doi.org/10.1002/micr.30505.
18. Weijs WLJ, Coppen C, Schreurs R, et al. Accuracy of virtually 3D planned resection templates in mandibular reconstruction. *J Craniomaxillofac Surg*. 2016;44:1828-1832.
19. Pompa G, Saccucci M, Di Carlo G, et al. A survival of dental implants in patients with oral cancer treated by surgery and radiotherapy: a retrospective study. *BMC Oral Health*. 2015;15(5). https://doi.org/10.1186/1472-6831-15-5.
20. Wijbenga JG, Schepers RH, Werker PMN, Witjes MJH, Dijkstra PU. A systematic review of functional outcome and quality of life following reconstruction of maxillofacial defects using vascularized free fibula flaps and dental rehabilitation reveals poor data quality. *J Plast Reconstr Aesthet Surg*. 2016;69:1024-1036.
21. Chen J, Yin P, Li N, Wu L, Jian X, Jiang C. Functional mandibular reconstruction with double-barrel fibular flap and primary osseointegrated dental implants improve facial esthetic outcome. *J Oral Maxillofac Surg*. 2019;77:218-225. https://doi.org/10.1016/j.joms.2018.08.008.
22. Allen RJ, Shenaq DS, Rosen EB, et al. Immediate dental implantation in oncologic jaw reconstruction: workflow optimization to decrease time to full dental rehabilitation. *Plast Reconstr Surg Glob Open*. 2019;7:e2100. https://doi.org/10.1097/GOX.0000000000002100.
23. Attia S, Wiltfang J, Pons-Kühnemann J, et al. Survival of dental implants placed in vascularised fibula free flaps after jaw reconstruction. *J Craniomaxillofac Surg*. 2018;46:1205-1210. https://doi.org/10.1016/j.jcms.2018.05.008.
24. Attia S, Wiltfang J, Streckbein P, et al. Functional and aesthetic treatment outcomes after immediate jaw reconstruction using a fibula flap and dental implants. *J Craniomaxillofac Surg*. 2019;47:786-791. https://doi.org/10.1016/j.jcms.2018.12.017.
25. Bodard AG, Salino S, Desoutter A, Deneuve S. Assessment of functional improvement with implant-supported prosthetic rehabilitation after mandibular reconstruction with a microvascular free fibula flap: a study of 25 patients. *J Prosthet Dent*. 2015;113:140-145.
26. Okay DJ, Buchbinder D. Implant rehabilitation and maxillomandibular free flap reconstruction. In: Kademani D, Tiwani P, eds. *Atlas of Oral & Maxillofacial Surgery*. 1st ed. Missouri: Elsevier; 2016:219-231.
27. Wu YQ, Huang W, Zhang ZY, Zhang ZY, Zhang CP, Sun J. Clinical outcome of dental implants placed in fibula-free flaps for orofacial reconstruction. *Chin Med J (Engl)*. 2008;121:1861.e5.
28. Schmelzeisen R, Neukam FW, Shirota T, Specht B, Wichmann M. Postoperative function after implant insertion in vascularized bone grafts in maxilla and mandible. *Plast Reconstr Surg*. 1996;97:719-725.
29. Bak M, Jacobson AS, Buchbinder D, Urken ML. Contemporary reconstruction of the mandible. *Oral Oncol*. 2010;46:71-76.
30. Pitak-Arnnop P, Hempricha A, Dhanuthaia K, Pausch NC. Fibular flap for mandibular reconstruction: are there old tricks for an old dog? *Rev Stomatol Chir Maxillofac*. 2013;114:15-18.
31. Chen R, Zhang H-Q, Huang Z-X, Li S-H, Zhang D-M, Huang Z-Q. Computer-assisted resection and reconstruction of bilateral osteoradionecrosis of the mandible using 2 separate flaps prepared from a single fibula. *Oral Maxillofac Surg*. 2018;126:2-106. https://doi.org/10.1016/j.oooo.2018.02.019.
32. Ganry L, Hersant B, Quilichini J, Leyder P, Meningaud JP. Use of the 3D surgical modelling technique with open-source software for mandibular fibula free flap reconstruction and its surgical guides. *J Stomatol Oral Maxillofac Surg*. 2017;118:197-202.
33. Toto JM, Chang EI, Agag R, Deravajan K, Patel SA, Topham NS. Improved operative efficiency of free fibula flap mandible reconstruction with patient-specific, computer-guided preoperative planning. *Head Neck*. 2015;37(11):1660-1664.
34. Hanasono MM, Skoracki RJ. Computer-assisted design and rapid prototype modeling in microvascular mandible reconstruction. *Laryngoscope*. 2013;123:597-604.
35. Antony AK, Chen WF, Kolokythas A, Weimer KA, Cohen MN. Use of virtual surgery and stereolithography-guided osteotomy for mandibular reconstruction with the free fibula. *Plast Reconstr Surg*. 2011;128:1080-1084.
36. Pompa G, Saccucci M, Di Carlo G, et al. Survival of dental implants in patients with oral cancer treated by surgery and radiotherapy: a retrospective study. *BMC Oral Health*. 2015;15:5. https://doi.org/10.1186/1472-6831-15-5.
37. Battaglia S, Ricotta F, Maiolo V, et al. Computer-assisted surgery for reconstruction of complex mandibular defects using osteomyocutaneous microvascular fibular free flaps: use of a skin paddle-outlining guide for soft-tissue reconstruction. A technical report. *J Craniomaxillofac Surg*. 2019;47:293-299.
38. Cornelius CP, Giessler GA, Wilde F, Metzger MC, Mast G, Probst FA. Iterations of computer- and template assisted mandibular or maxillary reconstruction with free flaps containing the lateral scapular border.

Evolution of a biplanar plug-on cutting guide. *J Craniomaxillofac Surg*. 2015;44:229-241. https://doi.org/10.1016/j.jcms.2015.11.005.
39. Tarsitano A, Battaglia S, Ramieri V, et al. Short-term outcomes of mandibular reconstruction in oncological patients using a CAD/CAM prosthesis including a condyle supporting a fibular free flap. *J Craniomaxillofac Surg*. 2017;45:330-337.
40. Schepers RH, Raghoebar GM, Vissink A, et al. Accuracy of fibula reconstruction using patient-specific CAD/CAM reconstruction plates and dental implants: a new modality for functional reconstruction of mandibular defects. *J Craniomaxillofac Surg*. 2015;43:649-657.
41. Goormans F, Sun Y, Bila M, et al. Accuracy of computer-assisted mandibular reconstructions with free fibula flap: results of a single-center series. *Oral Oncol*. 2019;97:69-75.
42. Pietruski P, Majak M, Swiatek-Najwer E, et al. Navigation-guided fibula free flap for mandibular reconstruction: a proof of concept study. *J Plas Rec Aest Surg*. 2019;72:572-580.
43. Ricotta F, Cercenelli L, Battaglia S, et al. Navigation-guided resection of maxillary tumors: can a new volumetric virtual planning method improve outcomes in terms of control of resection margins? *J Craniomaxillofac Surg*. 2018;46:2240-2247.
44. Schoen PJ, Reintsema H, Raghoebar GM, Vissink A, Roodenburg JLN. The use of implant retained mandibular prostheses in the oral rehabilitation of head and neck cancer patients. A review and rationale for treatment planning. *Oral Oncol*. 2004;40:862-871.
45. Barber AJ, Butterworth CJ, Rogers SN. Systematic review of primary osseointegrated dental implants in head and neck oncology. *Br J Oral Maxillofac Surg*. 2011;49:29-36.

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