



# Restoring Quality of Life: Assessing the Impact of Free Flap Reconstruction in Coronavirus Disease 2019-Associated Rhino-Orbital Mucormycosis Patients

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Indian J Plast Surg 2023;56:507–513.

## Abstract

**Background** In India, between May 5 and July 2021, 41,512 cases and 3,554 deaths due to mucormycosis were reported in coronavirus disease 2019 (COVID-19)-infected patients or COVID-19-recovered patients. COVID-19-associated rhino-orbital mucormycosis (CAROM) has been associated with adverse effects that can affect oral health, vision, and physical as well as emotional functioning. After the radical debridement of CAROM and antifungal therapy, reconstructive surgery should be employed to restore function and aesthetics; however, limited clinical data exist on its potential effect on the quality of life (QOL) of these patients.

**Objective** Our objective was to assess the QOL among CAROM patients reconstructed with free flap surgery.

**Materials and Methods** This analysis studied 19 patients of CAROM who had maxillectomy and/or orbital exenteration defects reconstructed with free flaps at a tertiary care center. All these patients were free from any residual disease, as confirmed by tissue biopsy taken from the affected area. The QoL of these patients was assessed 1 week preoperatively and 4 to 6 months postoperatively using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck Module (EORTC QLQ-HN43) questionnaire module.

**Results** There was a statistically significant improvement in 10 out of the total 19 parameters ( $p < 0.05$ ) which include pain in the mouth, problems opening mouth, speech, swallowing, weight loss, dry mouth and sticky saliva, body image, fear of progression, social contact, and social eating.

**Conclusion** The EORTC QLQ-HN43 questionnaire module presented a statistically significant improvement in the functional as well as psychological status of the CAROM patients undergoing reconstruction by free flap surgery.

## Keywords

- ▶ COVID-19
- ▶ free flap
- ▶ quality of life
- ▶ mucormycosis
- ▶ body image
- ▶ aesthetics

article published online  
October 16, 2023

DOI <https://doi.org/10.1055/s-0043-1776011>.  
ISSN 0970-0358.

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## Introduction

The coronavirus disease of 2019 (COVID-19), ushered in by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coronavirus, was officially declared a global pandemic by the World Health Organization in March 2020.<sup>1-4</sup> India has experienced three waves of COVID-19 since 2020, with the second wave in 2021 being the most devastating in every parameter.

The associated mucormycosis outbreak, often known as the “black fungus,” during the second COVID-19 wave led to an epidemic within a pandemic that resulted in extremely high morbidity and mortality in the nation.<sup>5-8</sup> In India, between May 5 and July 2021, 41,512 cases and 3,554 deaths due to mucormycosis were reported in COVID-19-infected patients or COVID-19-recovered patients.<sup>9</sup> In our institute between 30th April 2021 and 4th January 2022, 436 cases of COVID-19-associated mucormycosis were admitted. Out of these 436 cases, 99 patients succumbed to the disease. In total, 404 patients were diabetic.

Mucormycosis is classified into six clinical categories: rhino-orbital-cerebral mucormycosis, cutaneous, respiratory, gastrointestinal, and miscellaneous.<sup>10</sup> Uncontrolled diabetes mellitus, chronic use of steroids, candidates receiving organ transplants, neutropenia, and hematological cancers are risk factors for mucormycosis.<sup>11-13</sup>

To control the infection in patients with COVID-19-associated rhino-orbital mucormycosis (CAROM), aggressive and multiple radical debridement is necessary, along with antifungal therapy.<sup>14</sup> As a result, these patients are left with extensive facial defects, including missing orbital, mandibular, and palatal components, which lead to significant functional losses such as nasal breathing, oral feeding, and comprehensible speech. These defects can affect oral health, vision, and physical as well as emotional well-being. Once the infection is under control, it is vital to provide reconstructive options like free flap surgery that can enhance the quality of life (QOL) of these patients.<sup>15</sup>

Contrary to malignancy reconstruction, maxillectomy defects secondary to CAROM are repaired at a later stage. Therefore, the amount of fibrosis due to secondary contracture is greater, and the defect needs to be recreated. Additionally, the clear divisions of the components to be reconstructed are not well defined, as tissue components have contracted. Cancer patients need adjuvant radiotherapy in the postoperative period, so large-volume flaps are needed to counter flap contraction.<sup>16</sup> CAROM patients are not subjected to radiotherapy, so overcorrection and volume excess are not required.

CAROM patients have multiple comorbidities, such as diabetes mellitus and hypertension. Consequently, autonomic dysfunction can occur, leading to labile blood pressure both intraoperatively and postoperatively.<sup>17</sup> These factors pose challenges for both the operating surgeon and the anesthetist. Therefore, these patients require thorough monitoring both in the intraoperative and postoperative periods.

The assessment of patient satisfaction and QOL after reconstructive surgery is of paramount importance for these patients. However, at present, there are no data regarding the assessment of QOL in these patients. Therefore, this study

aimed to assess the potential effect on QOL among CAROM patients reconstructed with free flap surgery.

## Material and Methods

This was a prospective observational study conducted at a tertiary care hospital in India. The study was approved by the ethical committee of the institute. All procedures were performed in compliance with the institutional committee's ethical guidelines, the 1964 Helsinki Declaration and its later revisions, or other comparable ethical guidelines. This study comprises 19 cases of CAROM patients with maxillectomy defects or isolated orbital exenteration defects who underwent free flap reconstruction (►Fig. 1).

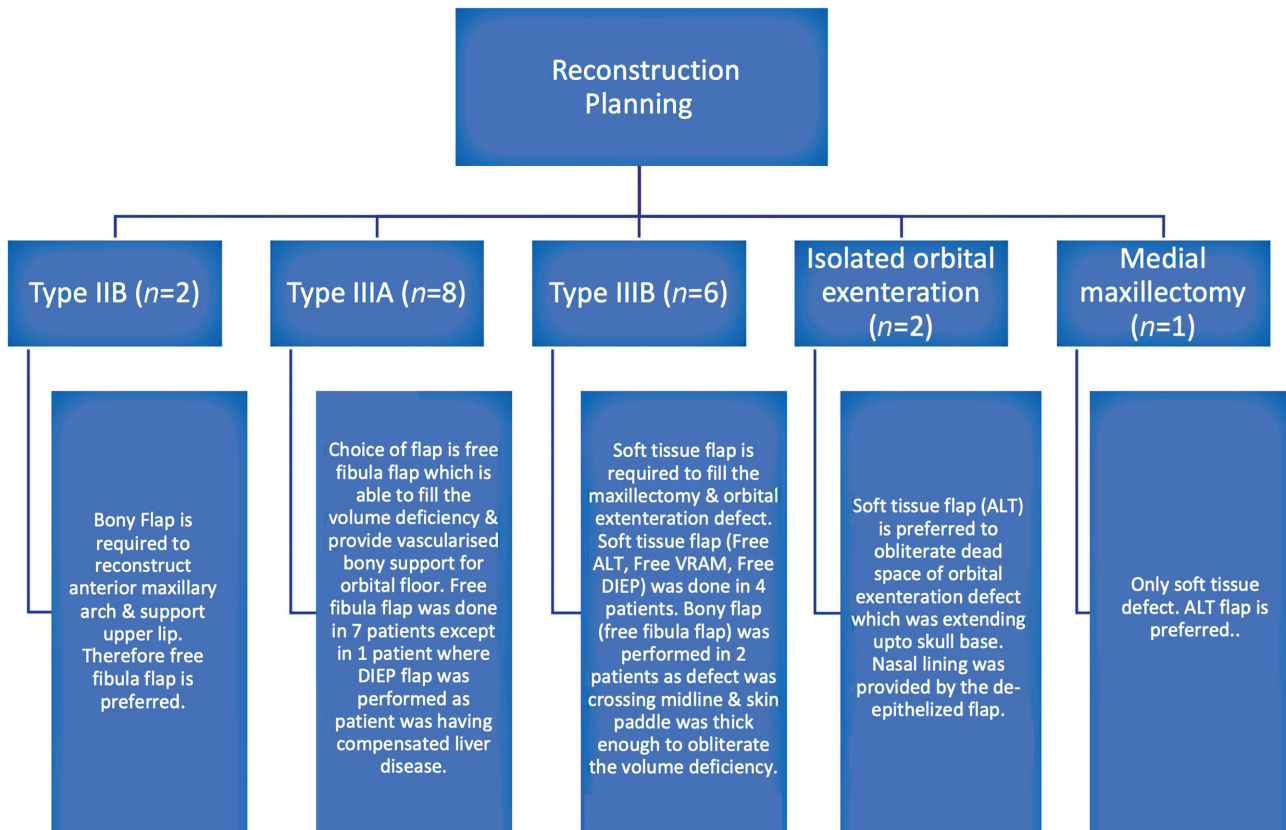
All patients who were free of any residual disease and planned for free flap reconstruction were included in the study. Patients who had any residual disease, patients who underwent immediate reconstruction after debridement, and patients who underwent reconstruction with pedicled flaps were excluded from the study.

The preoperative evaluation was done by the otolaryngology department to rule out any residual disease by taking a biopsy and performing magnetic resonance imaging of the affected area. Computed tomography imaging was requested for the affected region for surgical planning. After analyzing the imaging findings and considering factors such as the estimated volume and size of the defect as well as the patient's profile, a suitable free flap was selected for the reconstruction (►Fig. 1).

The classification of maxillectomy defects secondary to CAROM does not strictly follow the Cordeiro classification. We found that isolated unilateral orbital exenteration and medial maxillectomy have not been defined in the Cordeiro classification.<sup>18</sup> Moreover, our choice of flap had to be tailored not only to the defect but also to the patient's profile and preference. The choice of free flap for reconstruction in this study is depicted in ►Fig. 1.

The QOL of these patients was assessed 1 week before and 4 to 6 months after the surgery using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck Module (EORTC QLQ-HN43 questionnaire module).<sup>19</sup> The 43 questions in the EORTC QLQ-H&N43 have four options: “not at all,” “a little,” “quite a bit,” and “very much.” A Likert scale with four points was used to rate each item. The QLQ-HN43 module incorporates 19 symptom scales, which are made of 12 multi-item scales and seven single-item scales (►Tables 1 and 2).<sup>19</sup> The scores on all of the single-item and multi-item scales range from 0 to 100. A high score denotes a high degree of problem and thereby lower QOL. With approval from the appropriate authority, the Hindi version of the EORTC QLQ-H&N43 module was obtained and utilized.

Raw score and linear transformation score *S* of 19 parameters (12 multi-item scales and 7 single-item scales) in 19 patients were calculated preoperatively and postoperatively as provided by the EORTC QLQ-HN43 scoring manual.<sup>19</sup> Both the preoperative and postoperative linear transformation scores *S* were compared to assess the improvement in QOL in these patients.



**Data Collection**

Written informed consent was obtained from the patients. The EORTC QLQ-HN43 questionnaire module was handed over at preoperative and postoperative visits and was completed by them with the assistance of the nursing officer or the treating surgeons.

**Statistical Analysis**

Based on univariate analysis, the Wilcoxon signed-rank test was employed to compare the linear transformation score S of 19 patients before and after surgery. The results were regarded as statistically significant at  $p < 0.05$

**Results**

This study comprised 19 CAROM patients who underwent secondary reconstruction using free flaps. Out of 19 patients, 10 (52.63%) were male and 9 (47.36%) were female. The mean age in this study was 48 years (range: 32–64 years). In total, 11 (57.89%) patients had diabetes mellitus and hypertension. Out of 19 patients, 6 (31.57%) were hepatitis C virus positive.

**Table 1** Multi-item scales<sup>19</sup>

Parameter	Number of items (n)	Item range
1. Pain in the mouth	4	3
2. Swallowing	4	3
3. Problems with teeth	3	3
4. Dry mouth and sticky saliva	2	3
5. Problems with senses	2	3
6. Speech	5	3
7. Body image	3	3
8. Social eating	4	3
9. Sexuality	2	3
10. Problems with shoulder	2	3
11. Skin problems	3	3
12. Fear of progression	2	3

**Table 2** Single item scales<sup>19</sup>

Parameters	Number of items (n)	Item range
1. Problems opening mouth	1	3
2. Coughing	1	3
3. Social contact	1	3
4. Swelling in the neck	1	3
5. Weight loss	1	3
6. Problems with wound healing	1	3
7. Neurological problems	1	3



**Fig. 2** Type IIb maxillectomy defect.

Out of 19 patients with CAROM, 13 were using obturator prosthetic devices preoperatively. The types of facial defects and the types of free flaps used for reconstruction for these 19 patients are shown in **►Fig. 1**. None of the patients

included in this study required reexploration for microvascular thrombosis or hematoma (**►Figs. 2–5**).

In total, 10 out of the total 19 items of the EORTC QLQ-H&N43 questionnaire module showed statistically significant



**Fig. 3** Type IIIA maxillectomy defect.



**Fig. 4** Type IIIB maxillectomy defect.



**Fig. 5** Isolated orbital exenteration defect.

**Table 3** Improvement in quality of life in CAROM patients

Parameters	p-Value (<0.05) n = 19	p-Value (<0.05) n = 13 (using obturator)
<b>A. Multi-item scales</b>		
1. Pain in the mouth	0.0001	0.0001
2. Swallowing	0.0057	0.0001
3. Problems with teeth	0.340	0.381
4. Dry mouth and sticky saliva	0.0264	0.0001
5. Problems with senses	0.126	0.126
6. Speech	0.0001	0.0001
7. Body image	0.0018	0.0001
8. Social eating	0.0001	0.0001
9. Sexuality	0.606	0.711
10. Problems with shoulder	0.659	0.255
11. Skin problems	0.852	0.557
12. Fear of progression	0.0022	0.0001
<b>B. Single item scales</b>		
1. Problems opening mouth	0.0001	0.0001
2. Coughing	0.385	0.819
3. Social contact	0.0088	0.0001
4. Swelling in the neck	0.5028	0.819
5. Weight loss	0.008	0.008
6. Problems with wound healing	0.205	0.461
7. Neurological problems	0.5213	0.165

Abbreviations: CAROM, COVID-19-associated rhino-orbital mucormycosis.

improvement when the QOL was assessed postoperatively after free flap reconstruction in CAROM patients ( $p < 0.05$ ). The improvement in these 10 parameters was even present in the subgroup of patients who were using obturator prosthetic devices preoperatively (► **Table 3**).

## Discussion

In the literature, very few studies have been published assessing the QOL of maxillectomy patients.<sup>20–22</sup> In our study, we found statistically significant improvement in 10 parameters of the EORTC questionnaire module when comparing the QOL of CAROM patients who were using an obturator preoperatively and after free flap reconstruction. In a study by Roger et al comparing the prosthetic obturation and free flap in postmalignancy maxillectomy defects, no significant difference was found in the QOL of both groups.<sup>20</sup> The reason for this difference in outcome may be that survival is not a concern for CAROM patients once they have completed the primary treatment for the infection

and are free of residual disease, unlike patients with head and neck malignancies. Consequently, it was probably challenging for the patients in our series to come to terms with the fact that they would need to use a prosthesis for the next 30 to 40 years of their lives.

To improve the QOL of these patients, it is crucial to provide functional rehabilitation as well as a socially acceptable appearance. The functions that can be provided by reconstruction should include nasal breathing, oral feeding, and comprehensible speech. For an acceptable aesthetic appearance, the restoration of the volume of the face is essential. For patients with orbital exenteration, a reconstruction that makes use of eye prosthetics possible must be attempted.<sup>23</sup>

For volume restoration, free soft tissue flaps (free antero-lateral thigh, free vertical rectus abdominis musculocutaneous flap, and free deep inferior epigastric artery perforator flap) and free osteocutaneous flaps (free fibular osteocutaneous flap) are excellent options. The degree of freedom gained in inseting these flaps in complex 3D defects is much greater than that gained in pedicled flaps. The authors have also preferred a delayed reconstruction until the defect margins are confirmed negative for fungal infiltration.<sup>24–29</sup> This is because the angioinvasive property of the fungus can cause vascular thrombosis, which may compromise free flap survival.<sup>29</sup> Also, amphotericin-based antifungal therapy has severe and potentially lethal side effects. In our institute, 99 (22.7%) out of 436 admitted patients with CAROM died between April 2021 and January 2022. Providing immediate reconstruction with free flap surgery, which is a lengthy procedure, is not justifiable for this subgroup of patients because the mortality rate is very high.

In our study, we found a statistically significant improvement ( $p < 0.05$ ) in 10 items of the EORTC QLQ-H&N43 questionnaire module. Improvement in “problems of speech,” “swallowing,” and “dry mouth and sticky saliva” can be attributed to the reconstruction of the palate, thereby separating the oral and nasal cavities. Coverage of the large facial defect can prevent dryness of the oral and nasal mucosa, thereby improving the problem of “dry mouth.” Improvement in parameters of “body image,” “social contact,” “social eating,” and “fear of progression” of disease after reconstruction is because of the coverage of large three-dimensional facial defects. This gives the patient the ability to interact without dressings and masks and eat without a tube, leading to a more socially active life. The “pain in the mouth” and “problems opening mouth” are significantly reduced because of the release of long-standing scar tissue present in the oral cavity. Weight gain after surgery can be attributed to the change in type of feed postoperatively from liquid or tube feed to solid or semisolid diet.

In the current study on the Indian population, patients were conservative in answering the questions related to sexuality in the EORTC QLQ-H&N43 questionnaire module. Therefore, there can be bias in the responses to the questions related to sexuality.

Microvascular reconstruction in these patients is also challenging. The anastomosis was performed at the distal end of the facial vessels, which led to a mismatch between the

recipient and donor vessels. In general, the facial artery was friable, and intimal separation was found in five patients. We also found atherosclerosis in the flap artery in 11 patients.

The EORTC QLQ-H&N43 modules are very effective, dependable, and simple-to-use questionnaires to evaluate QOL postreconstruction. This module was formulated for head and neck cancer patients. Because of the lack of any standard questionnaire module for CAROM patients, the author has adapted the EORTC QLQ-HN43 questionnaire module in this study. The defect created after the radical debridement is similar to the defect after the resection of maxillary malignancy. Also, due to the large burden of CAROM patients in the country, many patients are requesting reconstructive surgery. Therefore, it is recommended that further studies are required and that a standard protocol and questionnaire module be formulated and published for assessing the QOL of CAROM patients undergoing reconstruction. The limitation of this study is the small sample size and use of the EORTC QLQ-H&N43 questionnaire for noncancer pathology. Longer follow-up periods are needed to validate these findings and explore additional factors affecting the QOL in these patients.

## Conclusion

In conclusion, CAROM patients experience significant functional and psychosocial challenges due to complex facial defects resulting from aggressive debridement to control the infection. Free flap surgery plays a crucial role in restoring function and improving the QOL of these patients.

**Conflict of Interest**  
None declared.

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