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**Research Paper** 

# EVALUATE THE CLINICAL OUTCOME OF THE SUCCESS RATE OF OSSEOINTEGRATED DENTAL IMPLANTS PLACED SECONDARILY IN FIBULA-FREE FLAPS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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#### Abstract

**Background and aim:** the present study conducted with the aim of evaluating the clinical outcome of the success rate of osseointegrated dental implants placed secondarily in fibula-free flaps.

**Method:** In present systematic review and meta-analysis, all articles published until the end of July 2023 through searching in databases PubMed, Scopus, Science Direct, ISI, Web of Knowledge, Elsevier, Wiley, and Embase and Google Scholar search engine were extracted using keywords and their combinations by two trained researchers independently. Data analysis was done using the fixed effects model in meta-analysis, by STATA (version 17); P-value less than 0.05 was considered significant.

**Result:** A total of ten studies were included in the meta-analysis process. Success rate of osseointegrated dental implants placed secondarily in Fibula-Free Flaps was 87% (ES: 95% CI, 70% to 86%;  $I^2$ =76.80; p=0.00).

**Conclusion:** Based on the present meta-analysis, a high success rate of osseointegrated dental implants placed secondarily in fibula-free flaps was observed. fibula free flap constitutes a standard therapy for jaw reconstructive surgery.

Keywords: Rehabilitation, Dental implant, Free fibula flap, Prosthodontics

Head and neck cancer, success rate

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### Introduction

In oral and maxillofacial surgery, one of the main and important components is reconstructive surgery. One of the most common defects in the maxillofacial skeleton is tumor ablation(1). Evidence shows that according to the nature of tumors, surgery can result in complex bone and soft tissue attachment defects(2). Options are available based on the size, location, extent of the involved tissues, the cause of the defect, such as vascularized flaps, non-vascularized autogenous grafts, or allogeneic materials that are used to reconstruct jaw and facial defects(3, 4). Studies have shown that vascularized flaps are one of the preferred options for reconstructing jaw and facial defects and they are obtained from different places such as the iliac crest, scapula, or fibula(5, 6). In the reconstruction of the lower jaw, the anatomy and function of the complex are effective on reconstructive surgery(7). In Maxilla, defects are classified into six classes(8). The purpose of reconstruction is to return function and shape to the state before the injury; It is also important to improve the quality of life of patients, their speech and chewing ability(9). Restoring chewing function and aesthetic results are the most challenging issues for dentists and patients. The evidence shows that the use of implantsupported prostheses are better options in the repair of complex oral and facial defects(10, 11). Fibula osseous was introduced for maxillomandibular reconstruction in 1989 and has advantages that make its use ideal(12). Implants can be placed at the time of the primary maxillary or mandibular reconstruction or as a second step, months after the primary reconstruction(13). Several factors affect the success of the implant (implant stability, bone loss around the implant, hard and soft tissue, pain and infection). The success of the implant allows patients to function properly(14). The inconsistency in the results of using free flaps and the time of implantation and the amount of implant failure in different studies led the present study to provide evidence in this field by examining the findings of the studies. Therefore, the present study conducted with the aim of evaluating the clinical outcome of the success rate of osseointegrated dental implants placed secondarily in fibula-free flaps.

### Method

### Search strategy

In present study, in order to obtain scientific documents and clinical outcome of osseointegrated dental implants, articles published in international databases such as PubMed, Web of Science, Scopus, Science Direct, Web of Knowledge, EBSCO, Wiley, ISI, Elsevier, Embase and Google Scholar search engine were used. The search process until July 2023 in PubMed database was done using MeSH keywords: ((((("Prostheses and Implants"[Mesh] OR "Dental Implants" [Mesh]) OR "Dental Implantation" [Mesh]) OR "Dental Implantation, Endosseous, Endodontic"[Mesh]) AND "Mandibular Reconstruction"[Mesh]) OR "Maxilla"[Mesh]) OR ( "Mandible"[Mesh] OR "Mandibular Prosthesis Implantation"[Mesh] ) OR ("Mandibular Reconstructive Surgery" [Mesh]) OR ("Reconstructive Surgeries, Mandibular"[Mesh]) OR ("Maxillo-Mandibular Reconstruction"[Mesh]) OR ("Reconstruction, Maxillo-Mandibular" [Mesh]) AND ("Fibula" [Mesh]). In addition, the reference list of the obtained articles was checked to identify the used articles that were not obtained using the above methods. Databases were searched with high sensitivity. To avoid bias, the search was done by two researchers independently.

### Study selection criteria

Inclusion criteria: use of the PIO (patient/population, intervention, and outcome) strategy to construct the research question is specified in Table 1; maxillary and or mandibular reconstruction, reported success rate, free fibula flaps, delayed implant placements, English language. studies with incomplete results; in-vitro, in-vivo, animal studies, case reports, editorial and review articles were excluded.

| Table1. PIO strat | legy.   |
|-------------------|---|
| PICO strategy     | Description   |
| Р                 | Population: patients who underwent reconstruction surgery             |
| Ι                 | Intervention: Dental implants placed secondarily in fibula-free flaps |
| 0                 | Outcome: clinical outcome and success rate                            |

# Data collection

a checklist was designed based on the objectives, and information from the selected articles was entered into the checklist (Table 2).

### Risk assessment

Cochrane Collaboration tool to assess risk of bias for randomized controlled trials. Bias is assessed as a judgment (high, low, or unclear)(15). The risk of bias tool covers six domains of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other. The scores of this tool are between 0 and 6, and higher score showed higher quality of study; the scoring of each item is 1 for low risk and 0 for high and unclear risk.

Newcastle-Ottawa Scale (NOS) (16) used to assessed quality of the cohort and cross-sectional studies, case-control and case series studies, This scale measures three dimensions (selection, comparability of cohorts and outcome) with a total of 9 items. In the analysis, any studies with NOS scores of 1-3, 4-6 and 7-9 were defined as low, medium and high quality, respectively. *Data analysis* 

# Data analysis

Meta-analysis was performed using effect size with 95% confidence interval. To estimate the heterogeneity of the studies, the index  $I^2$  (<25%: weak heterogeneity, 25-75%: moderate heterogeneity, and more than 75%: high heterogeneity) was used. The results were combined using the fixed effect model (Inverse–variance method) in meta-analysis. The publication bias was checked by Egger test and data analysis was done using STATA/MP. v17 software. A p-value of less than 0.05 was considered significant.

#### Result

After searching with related keywords, 414 studies were obtained. Endnote.X8 software was used to organize the studies. By using the mentioned software and reviewing the title and abstract of the articles, 81 duplicate studies were eliminated. Then the abstracts of 319 articles were examined by the researchers. 285 studies that did not meet the inclusion criteria or were excluded due to weak or unrelated relevance to the study objective (if after reading the title and abstract, it was not possible to make a decision about the article, the full text was referred to). The full text of 34 articles was carefully reviewed by two independent researchers, and 24 studies were excluded due to the inconsistency of study objectives; Finally, ten articles were selected (Figure 1).

# Characteristics of patients

305 (female: 103; male:202) patients who underwent maxillary and or mandibular reconstruction with free fibula flaps included in present study. The number of implants in total was 994. Characteristics of selected studies reported in table 2.

### Risk of bias assessment

According to Cochrane Collaboration tool one RCT study (17) had low risk of bias (4/6); and according to NOS tool, four studies had low risk of bias (7,8/9) and five studies had moderate risk of bias (5,6/9).

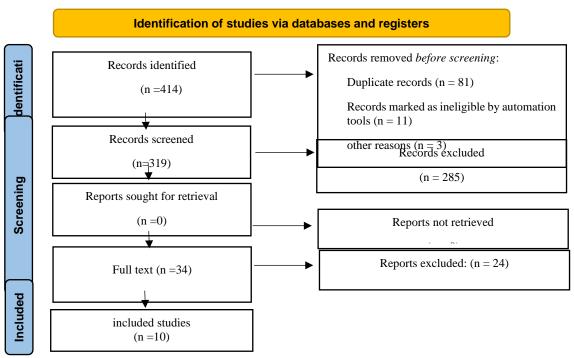


Figure 1. PRISMA 2020 Checklist.

| No. | Study. Years                    | Study design  | Number of Patients |        | Mean or      | Number of | Type of       |    | Bias       |     |
|-----|---------------------------------|---------------|--------------------|--------|--------------|-----------|---------------|----|------------|-----|
|     |                                 |               |                    |        | range of age | Implants  | pathology (n) |    | assessment |     |
|     |                                 |               | male               | female | (years)      |           | Ma            | Be | Tra        |     |
| 1   | Jeong et al., 2022<br>(18)      | Retrospective | 11                 | 10     | 14-75        | 100       | 18            | 3  | -          | 7/9 |
| 2   | Lodders et al.,<br>2021(19)     | Retrospective | 23                 | 21     | 60.3         | 161       | 40            | 4  | -          | 8/9 |
| 3   | Knitschke et al.,<br>2021 (20)  | Retrospective | 25                 | 11     | 59.9         | 36        | 30            | 6  | -          | 7/9 |
| 4   | Attia et al., 2018<br>(21)      | Retrospective | 23                 | 11     | 17-79        | 134       | 27            | 7  | -          | 6/9 |
| 5   | Pellegrino et al.,<br>2018 (22) | Retrospective | 15                 | 6      | 50           | 108       | 15            | 6  | -          | 7/9 |
| 6   | Kumar et al., 2016<br>(17)      | RCT           | 26                 | 8      | 33.95        | 104       | 10            | 24 | -          | 4/6 |
| 7   | Jain et al., 2017 (23)          | Retrospective | 5                  | 5      | 18-59        | 33        | -             | 10 | -          | 6/9 |
| 8   | Wang et al., 2015<br>(24)       | Retrospective | 12                 | 7      | 28-55        | 51        | -             | 19 | -          | 6/9 |

| 9  | Fang et al., 2015 | Retrospective | 61 | 13 | 19-75 | 192 | 47 | 9  | 18 | 5/9 |
|----|-------------------|---------------|----|----|-------|-----|----|----|----|-----|
|    | (25)              |               |    |    |       |     |    |    |    |     |
| 10 | Chiapasco et al., | Retrospective | 1  | 11 | 51-68 | 75  | -  | 12 | -  | 6/9 |
|    | 2011 (26)         |               |    |    |       |     |    |    |    |     |

Ma: Malignant; Be: Benign; Tra: Trauma

### Implant success rates

Success rate of osseointegrated dental implants placed secondarily in Fibula-Free Flaps was 87% (ES: 95% CI, 70% to 86%;  $I^2$ =76.80; p=0.00) (Fig.2).

| Study  |      | Implant success rates<br>with 95% Cl | Weight<br>(%) |
|--|------|--------------------------------------|---------------|
| Jeong et al., 2022                                     |      | - 0.82 [ 0.23, 1.41]                 | 1.69          |
| Lodders et al., 2021                                   |      | 0.40 [ 0.20, 0.60]                   | 15.19         |
| Knitschke et al., 2021                                 |      | 0.43 [ 0.23, 0.63]                   | 15.19         |
| Attia et al., 2018                                     |      | — 0.91 [ 0.32, 1.50]                 | 1.69          |
| Pellegrino et al., 2018                                |      | 0.98 [ 0.78, 1.18]                   | 15.19         |
| Kumar et al., 2016                                     |      | 0.97 [ 0.58, 1.36]                   | 3.80          |
| Jain et al., 2017                                      |      | 0.93 [ 0.73, 1.13]                   | 15.19         |
| Wang et al., 2015                                      |      | — 0.86 [ 0.27, 1.45]                 | 1.69          |
| Fang et al., 2015                                      |      | 0.90 [ 0.70, 1.10]                   | 15.19         |
| Chiapasco et al., 2011                                 |      | 0.96 [ 0.76, 1.16]                   | 15.19         |
| Overall  | •    | 0.78 [ 0.70, 0.86]                   |               |
| Heterogeneity: $I^2 = 76.80\%$ , $H^2 = 4.31$          |      |                                      |               |
| Test of $\theta_i = \theta_j$ : Q(9) = 38.80, p = 0.00 |      |                                      |               |
| Test of θ = 0: z = 19.99, p = 0.00                     |      |                                      |               |
| r<br>O   | .5 1 | 1.5                                  |               |
| Fixed-effects inverse-variance model                   |      |                                      |               |

Figure 2. forest plot showed implant success rates

#### Implant failure rate

failure rate of osseointegrated dental implants placed secondarily in Fibula-Free Flaps was 14% (ES: 95% CI, 6% to 22%; I<sup>2</sup>=60.12; p=0.01) (Fig.3).

| Study  |            | Implant failure rate<br>with 95% CI | Weight<br>(%) |
|--|------------|-------------------------------------|---------------|
| Jeong et al., 2022                                     |            | 0.18 [ -0.41, 0.77]                 | 1.69          |
| Lodders et al., 2021                                   |            | 0.06 [ -0.14, 0.26]                 | 15.19         |
| Knitschke et al., 2021                                 | — <b>—</b> | 0.57 [ 0.37, 0.77]                  | 15.19         |
| Attia et al., 2018                                     |            | 0.09 [ -0.50, 0.68]                 | 1.69          |
| Pellegrino et al., 2018                                |            | 0.02 [ -0.18, 0.22]                 | 15.19         |
| Kumar et al., 2016                                     | <b>_</b>   | 0.03 [ -0.36, 0.42]                 | 3.80          |
| Jain et al., 2017                                      |            | 0.07 [ -0.13, 0.27]                 | 15.19         |
| Wang et al., 2015                                      |            | 0.14 [ -0.45, 0.73]                 | 1.69          |
| Fang et al., 2015                                      |            | 0.10 [ -0.10, 0.30]                 | 15.19         |
| Chiapasco et al., 2011                                 |            | 0.04 [ -0.16, 0.24]                 | 15.19         |
|  | <b>•</b>   | 0.14 [ 0.06, 0.22]                  |               |
| Heterogeneity: $I^2 = 60.12\%$ , $H^2 = 2.5\%$         | 1          |                                     |               |
| Test of $\theta_i = \theta_j$ : Q(9) = 22.57, p = 0.01 |            |                                     |               |
| Test of $\theta$ = 0: z = 3.56, p = 0.00               |            | _                                   |               |
|  | 5 0 .5     | י<br><b>1</b>                       |               |
|  |            |                                     |               |

Fixed-effects inverse-variance model

Figure 2. forest plot showed implant failure rate

### Discussion

In the present study, the success of dental implants placed secondarily in free fibula flaps was reported. Based on the present meta-analysis, high success rates were observed (78%), which shows that dental implants placed secondarily in free fibula flaps can successfully osseointegrate and be used for dental rehabilitation. Also, the implant failure rate was 14%, which shows that the use of this method is effective in the long follow-up period. However, the heterogeneity between studies was high and the findings of the present study should be interpreted with caution; One of the reasons for this heterogeneity was the remote follow-up of the variable in the studies, and another reason is the difference in the cognitive methodology of the studies. In line with the results of the present study, a study showed 91.9% survival rates in the ten-year follow-up period(27). Also, another study reported 5%, 87% at 1 year and 5year cumulative success rate, respectively(28). Most studies have only reported implant survival rates, with heterogeneities in the definition of implant success rate(29). Success rate has mostly been defined as the absence of implant-related pain, suppuration, swelling, mobility, discomfort, ongoing pathological processes, peri-implantitis, neuropathies, or persistent paresthesia, as noted by van Steenbergher(30). Cabbar et al., 2018 reported a fibula flap implant success rate of 92.6%(31); Sandoval et al., 2020 reported a 93% implant success rate(32); and Pellegrino et al. reported 1-, 5-, and 10-year implant success rates of 95.4%, 73.5%, and 64.7%, respectively(22). One systematic review of 910 implants placed in vascularized fibular grafts determined a 40-month success rate of 92.6% (82-100%)(13). Implants placed in fibula flaps had an estimated 94% success rate(4).

The literature provides several reasons for failure of dental rehabilitation, including microstomia, unfavorable maxillomandibular relations, and dental implant failure(33). Identifying functional dental rehabilitation is difficult because an implant-supported prosthetic construction may serve different purposes in head and neck cancer patients. for example, cosmetic and/or functional. According to studies, there are reconstructed patients who still cannot masticate properly after completing implant-based dental rehabilitation. On the other hand, these patients are satisfied with their prosthetic device because it fulfills a clear cosmetic function when participating in society(19).

Bone grafting with significant continuity defects can be very challenging due to the risk of resorption, exposure, infection and ultimately graft loss, therefore, the selection of bone graft should be based on criteria such as the size and type of defect, the type of tissue lost. , the need for auxiliary treatment and the health status of the patient(26, 34). Factors can affect the success rate of dental implants, such as radiotherapy used as an adjuvant treatment. challenging factors in these series, such as a high percentage of stage IV disease, extensive bone defects, and a high number of irradiated patients, could explain why almost a quarter of the dental implants were not functional(19).

The present study had limitations, firstly, only one RCT study was found and the other studies were conducted retrospectively; More RCT studies need to be conducted to confirm the evidence with cognitive methodology and follow-up period appropriate to other studies.

#### Conclusion

Based on the present meta-analysis, a high success rate of osseointegrated dental implants placed secondarily in fibula-free flaps was observed. fibula free flap constitutes a standard therapy for jaw reconstructive surgery. The present meta-analysis of 305 patients who

underwent maxillary and or mandibular reconstruction with free fibula flaps shows a cumulative success rate of 78%. More prospective and RCT studies are needed to better evaluate the long-term results of implant implantation in free fibula flaps to confirm the evidence of the present study due to the high heterogeneity obtained.

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