

What Is the Success of Implants Placed in Fibula Flap? A Systematic Review and Meta-Analysis

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ABSTRACT

Objectives: The purpose of this systematic review and meta-analysis is to examine the success rate of osseointegrated dental implants placed secondarily in fibula free flaps using the Albrektsson and colleagues criteria.

Material and Methods: A computerized database search was performed using PubMed, Embase, Web of Science and Cochrane CENTRAL. Specific ascertainment criteria were applied for the inclusion of the eligible studies. This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis PRISMA checklist. Risk of bias was assessed for all the included studies.

Results: The meta-analysis was carried using ten studies that met the inclusion criteria. The present review pooled data obtained from 242 patients (167 males and 75 females), with the age range of 13 to 79 years. A total of 848 dental implants were placed in the free fibula flaps. All dental implants were placed in a delayed fashion, ranging from 14 to 192 months. The estimated proportion of successful implants placed in fibula flaps used to reconstruct the maxillomandibular complex was 0.94 or 94% (95% CI [confidence interval] = 0.91 to 0.96) with an insignificant heterogeneity of 37%, $P = 0.12$. Using a random effect model the annual implant failure rate was 0.02 with a 95% CI = 0.01 to 0.03.

Conclusions: The results of this systematic review and meta-analysis strongly indicate that using objective criteria, delayed implant placement in free fibula flaps is highly successful.

Keywords: dental implants; free tissue flaps; mandibular reconstruction; meta-analysis; prostheses and implants; vascular graft occlusion.

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INTRODUCTION

Reconstructive surgery is a major and crucial component of oral and maxillofacial surgery specialty. The maxillofacial skeleton is subject to several types of defects secondary to trauma, craniofacial/congenital deformities, and tumour ablation [1]. The latter constitutes the most common cause of orofacial defects. Given the nature of tumours, ablative surgery results in complex continuity defects of bone and soft tissues. Orofacial defects impact both the form and function of the most prominent and complex body part, the face [2,3].

Various options such as vascularized flaps, non-vascularized autogenous grafts, or allogeneic materials are available to reconstruct maxillofacial defects. They are utilized based on the size, location, extent of the tissues involved, the cause of the defect, and the host environment. Owing to the vascularized graft's superior outcomes and versatility, for a critical sized bone continuity defects of the maxilla or the mandible vascularized grafts is the preferred option. Vascularized bone can be obtained from various sites such as the iliac crest, the scapula, or the fibula, among others [4,5].

The complex anatomy and function of the maxillomandibular complex impacts the choice of reconstruction of the maxillofacial defects. Various classification systems have been developed over the years that aim to guide reconstructive options based on the units resected and functions impacted. Maxillary defects are classified into six classes; I to IV delineates maxillary defects in the vertical dimensions, while class V and VI describe orbitomaxillary and nasomaxillary defects, respectively [6]. Mandibular defects are classified according to the body's HCL classification in which H defects represent lateral defects including the condyle, the same for L defects except the condyles are not affected, and finally, C defects that represent a defect of the entire central segments including incisor and canine teeth [7]. The ultimate goal of any reconstruction is to restore form and function ideally to the "pre-injury" or "pre-disease" state. For the maxillomandibular complex specifically, function includes speech and mastication. The ability to chew and articulate properly dramatically impacts the quality of life of the patients [8-12].

Historically, removable dental prostheses to restore ablative or traumatic defects posed several challenges for dental practitioners and patients in terms of restoring masticatory function and aesthetic outcomes. Stability and retention of the removable prostheses

remains a major challenge with these complex defects. Dental implants, on the contrary, allow for the fabrication of prostheses that have superior retention, support, and function. Implant-supported prostheses are quite versatile and thus are superior in the restoration of various complex orofacial defects [13-17].

The fibula osseous or osseo-myocutaneous flap has been the workhorse for maxillomandibular reconstruction since it was first introduced by Hidalgo in 1989 [18]. Some of the major advantages of the fibula over other flaps include the length of bone that can be harvested, that makes it ideal for large sized defects; furthermore it can be harvested with or without soft tissues. Additionally, the length of the vessel pedicle allows for anastomosis to the neck vessels without the need for inter-positional grafting [5]. Osteotomies can be placed in the fibula to mimic the shape and contour of the mandible and maxilla, and it also allows the placement of dental implants. Implants can be placed at the time of the primary reconstruction of the maxilla or the mandible or as a second stage, months after the primary reconstruction [13]. Numerous studies have reported "high success rates" of implants placed in free fibula flaps [2,13,16,19-45]. Regardless of the timing of placement, the success of an implant implies that it can be ultimately restored so patients can function appropriately. The criteria proposed by Albrektsson and co-workers [46] in 1986, provides one of the most comprehensive and objective manner to evaluate for the implant success. The Albrektsson et al. [46] criteria evaluates all aspects related to implant success, including implant stability, peri-implant bone loss after the first year of use, peri-implant hard and soft tissue health, and patient-related factors including pain and infection or any other symptoms that would affect the success of the implants. The ideal timing of dental implant placement in free flaps and how success is best defined are not consistent throughout the literature.

This systematic review and meta-analysis aims to examine the success rate of osseointegrated dental implants placed secondarily in fibula free flaps using one of the most comprehensive and objective approach, that is by applying the Albrektsson and colleagues proposed criteria [46].

MATERIAL AND METHODS

Protocol and registration

This systematic review adhered to the Preferred Reporting Items for Systemic Reviews and Meta-

analysis PRISMA checklist (<http://prisma-statement.org>). This study didn't require Institutional Review Board approval. The authors have read the Helsinki Declaration and have followed the guidelines in this investigation.

Focus question

The focus question was developed according to the Patient, Intervention and Outcome (PIO) framework as described in Table 1.

Focus question: what is the success rate of dental implant placement in delayed fashion in the free fibula flaps using the Albrektsson and colleagues criteria [46]?

Information sources

An electronic systematic search was performed, without any restrictions on the publication dates. The language was restricted to English. Following

databases were searched: PubMed, Embase, Web of Science and Cochrane CENTRAL. The time frame for the published articles was from January 1992 to September 2020.

Search

The search strategy was developed for PubMed and revised appropriately for each database. Details of the search for each database are provided in Table 2.

Selection of studies

PRISMA flow chart represents an outline of the selection process (Figure 1). The titles and abstracts of all identified studies were screened by two independent reviewers (AK and MA). Duplicates were removed, followed by the assessment of full texts. Differences between reviewers were addressed by discussion and consensus.

Table 1. PIO guidelines

Patient and population (P)	Patients who underwent maxillary and or mandibular reconstruction with free fibula flaps.
Intervention (I)	Dental implant placement in delayed fashion.
Outcomes (O)	Success rate using the Albrektsson et al. [46] criteria?
Focused question	What is the success rate of dental implant placement in delayed fashion in the free fibula flaps using the Albrektsson et al. [46] criteria?

Table 2. Database search strategy. Relevant subject heading (MeSH) terms and keywords

Database	Search Strategy	Results retrieved
PubMed	(Maxillo-Mandibular Reconstruction OR ((Mandible OR Mandibular OR Maxilla OR Maxillary) AND (Reconstruct* OR defect*))) AND (Fibula OR Fibula*) AND (Dental Implants OR Dental Implantation OR Dental Implantation, Endosseous) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) NOT ("Case Reports" [Publication Type] OR "Comment" [Publication Type] OR "Editorial" [Publication Type] OR "Letter" [Publication Type]) Filters: English	198
Embase	('fibula'/exp OR fibula) AND ('mandible'/exp OR mandible OR 'maxilla'/exp OR maxilla OR 'jaw, upper' OR 'maxilla' OR 'maxillary' OR 'maxillary area' OR 'maxillary growth' OR 'maxillofacial skeleton' OR 'upper jaw') AND ('tooth implant'/exp OR 'bicon' OR 'grafton' OR 'swish active' OR 'swish tapered' OR 'dental implant' OR 'dental implants' OR 'implant, teeth' OR 'implant, tooth' OR 'implants, teeth' OR 'implants, tooth' OR 'teeth implant' OR 'teeth implants' OR 'tooth implant' OR 'tooth implants' OR 'tooth implantation'/exp OR 'apertognathia' OR 'blade implantation' OR 'dental implantation' OR 'dental implantation, endosseous' OR 'dental implantation, endosseous, endodontic' OR 'dental implantation, subperiosteal' OR 'immediate dental implant loading' OR 'tooth implantation') AND [english]/lim NOT 'case report'/de	245
Web of Science	TS=((Mandib* OR Maxill*) AND (Reconstruct* OR defect*)) AND TS=(Fibula*) AND TS= (Dental Implant*) Refined By:[excluding]: DOCUMENT TYPES: (MEETING OR EDITORIAL OR LETTER OR CASE REPORT OR ABSTRACT OR PATENT OR BOOK) AND LANGUAGES: (ENGLISH) Databases= WOS, BCI, CCC, DRCI, DIIDW, KJD, MEDLINE, RSCI, SCIELO, ZOOREC Timespan=All years Search language=English	298
Cochrane CENTRAL	fibula* in All Text AND implant* in All Text AND mandib* OR maxill* in All Text (Word variations have been searched)	18

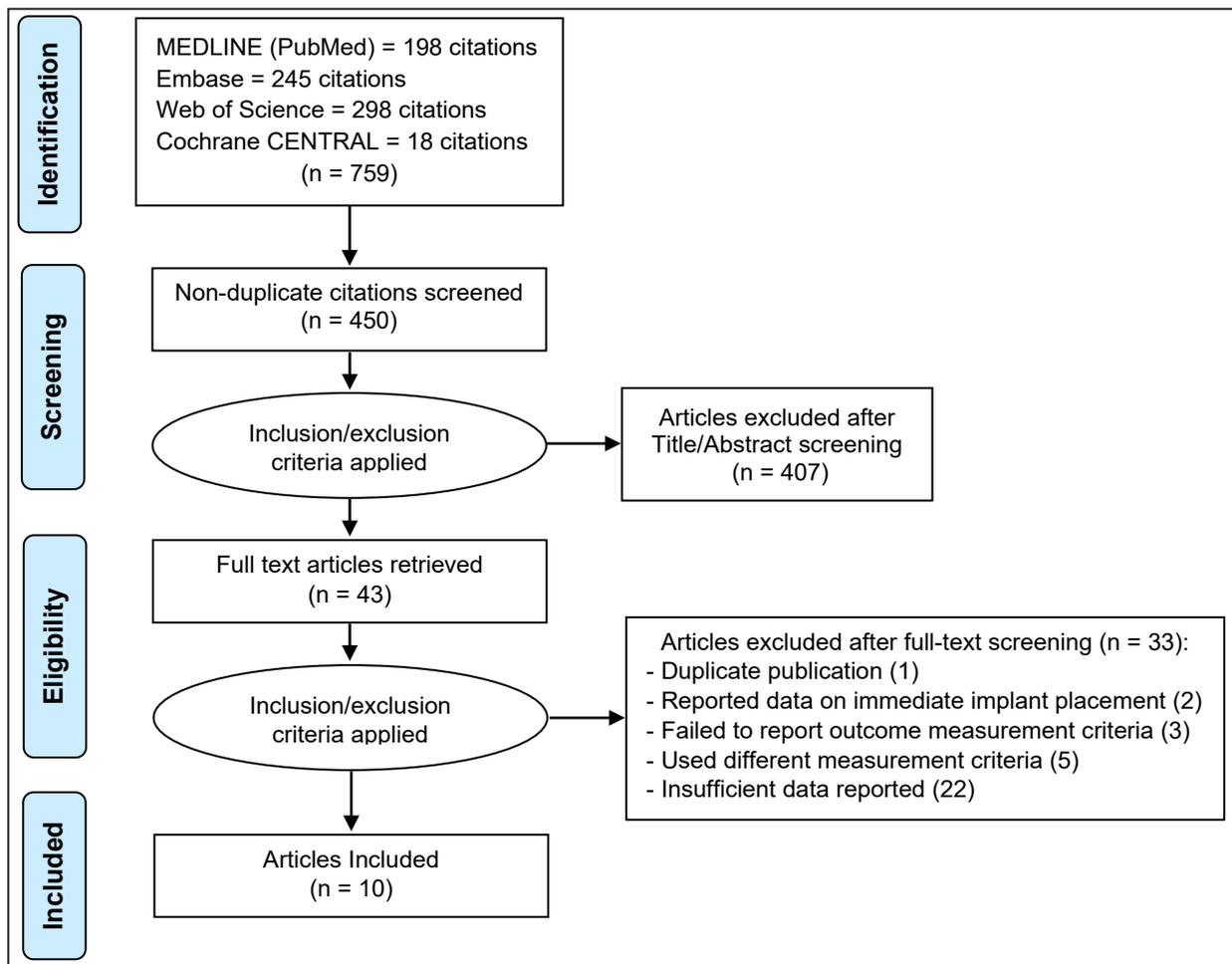


Figure 1. PRISMA flow diagram.

Furthermore, the reference list of all eligible articles identified in the databases was searched for additional pertinent studies.

Types of publications

The studies included were limited to randomized clinical trials, prospective studies, retrospective studies, that reported on dental implant placement in free fibula flaps (maxilla and /or mandible) in humans. Abstracts, reviews, editorials, comments, and guidelines were excluded.

Types of participants

Patients who had dental implants placed in the free fibula flaps used for reconstruction of maxillary and or mandibular defects.

Inclusion and exclusion criteria

Inclusion criteria

Only full-length articles were included. The studies included were limited to randomized clinical trials,

prospective studies, retrospective studies, that reported on dental implant placement in free fibula flaps (maxilla and/or mandible) in humans. Furthermore, studies that evaluated outcomes using the Albrektsson et al. [46] criteria and followed patients for at least one year were included. The language was restricted to English.

Exclusion criteria

Abstracts, reviews, editorials, comments, case reports, methodologies, and guidelines were excluded. Insufficient data to evaluate outcome parameters such as timing of implant placement and follow-up less than one year were not included.

Studies in which implants were not prosthetically restored were excluded as well.

Data extraction

The data were independently extracted by the authors (AK, PG and MA) using a previously prepared data extraction form. Any discrepancies were resolved by discussion.

Data items

Data on the following variables were collected: author, year of publication, study design, number of patients, age, gender, number of implants (success and failed), type of pathology treated (malignant, benign, trauma), and criteria for outcome measures.

Statistical analysis

Data extraction was completed using Microsoft Office Excel Version 2016 (Microsoft Corporation; Washington, USA).

For each study involved, successful implant counts were divided over total implants reported to generate the proportion of successful implants. With each of the study's success proportion estimates, standard errors were calculated to obtain the 95 percent confidence intervals (95% CI) of the summary estimates of the proportion of the succeeded implants.

Heterogeneity between studies for both implant failure rate and success proportion was assessed using I-squared (I^2) statistics describing the variation in implant failure and proportion of implant successes, which is attributable to the heterogeneity of the studies. All statistical analyses were performed using metaphor and meta-packages of R Statistical Software version 4.1.2 (R Foundation for Statistical Computing; Vienna, Austria), and level of statistical significance (alpha level) was based at 0.05.

The 95% CI for the implant failure rate and success proportion was then calculated by using the 95% confidence limits of the failure success proportions. The R Statistical Software computed the I^2 statistic to assess the heterogeneity between studies and the associated P-value. Heterogeneity (goodness-of-fit) with P-value below 0.05 was regarded as significantly lack of heterogeneity and heterogeneity (goodness-of-fit) with P-value above 0.05 was regarded as presence of heterogeneity.

A random effects model was generated due to variations in the implant failure rate and proportion of the implant successes among the included students. The model was used to do meta-analysis of the implant failure rate and proportion of implant successes reported in the included studies. With this model, differences between studies account for variability and not just due to random error. Therefore, studies with smaller sample sizes do not greatly affect the weight of each study.

Risk of bias in included studies

The assessment of the risk of bias in the included

studies was undertaken independently by same authors (AK and MA) and was performed in accordance with the approach based on the Center of Evidence-Based Medicine, Critical Appraisal of Prognostic Studies worksheet (<https://www.cebm.ox.ac.uk/resources/ebm-tools/critical-appraisal-tools>).

RESULTS

Study selection

The literature search generated 759 articles. Following de-duplication, titles and abstracts of 450 articles were screened. Of these 450 articles, 407 did not meet the inclusion criteria and were excluded. Forty-three articles remained for the full-text analysis and out of these, 10 articles met the inclusion criteria [3,17,45,47-53]. Thirty-three articles were excluded due to lack of the following: different criteria for outcome measures, implants not restored, follow-up less than 12 months, immediate implant placement, inadequate power to conduct an analysis, failure to report the criteria used to measure the outcomes. Two articles used periotest to measure implant stability with follow-up less than 12 months, three articles used resonance frequency analysis. Three articles failed to report specific criteria for outcome measurement, and finally, 2 articles were excluded as they reported data on immediate implant placement. One article was noted to be a duplicate and was removed. Twenty-two articles were excluded as they did not have sufficient data [2,20,26,31,36,43,44,54,55]. Article review and data extraction were performed according to the PRISMA flow diagram (Figure 1).

Quality assessment

The quality of the included studies is summarized in Figure 2. The assessment of the risk of bias was performed in accordance with the approach based on the Center of Evidence-Based Medicine, Critical Appraisal of Prognostic Studies worksheet (<https://www.cebm.ox.ac.uk/resources/ebm-tools/critical-appraisal-tools>).

Out of ten studies, nine studies were grouped together and included for the quality assessment [3,17,45,47-52]. One study by Kumar et al. [53] which was a randomized clinical trial was not included in this group. Only studies (retrospective or prospective) with similar design were analyzed. The quality of the randomized clinical trial was evaluated and noted to be good [53]. Four studies were considered having low risk of bias [48-51], and five studies recorded high risk of bias [3,17,45,47,52].

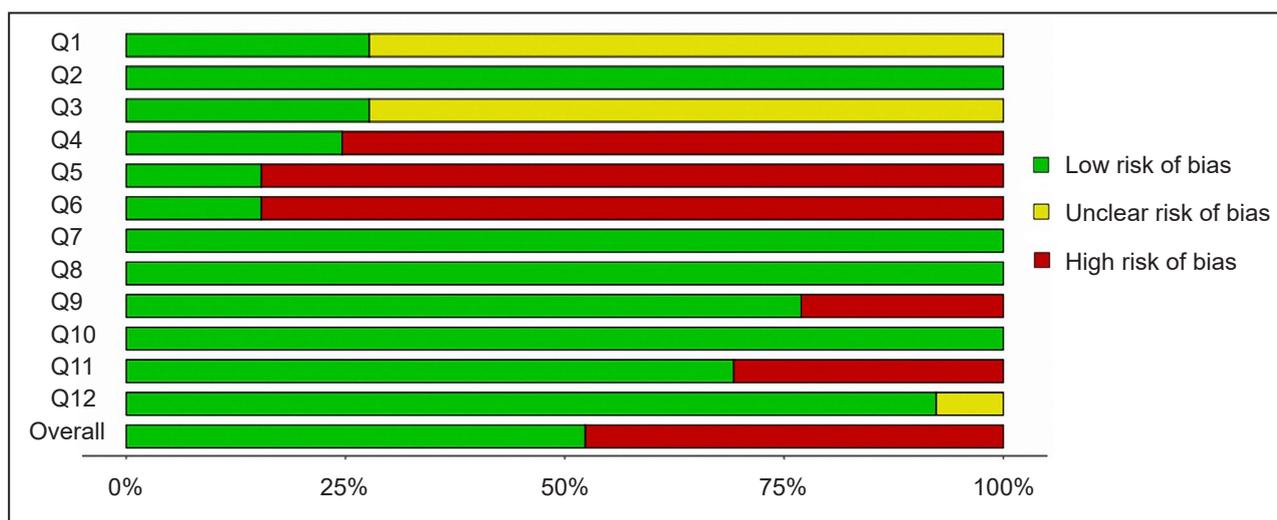


Figure 2A. Quality assessment and risk of bias summary graph.

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Overall
Roumanas et al. [3]	⊖	⊕	⊖	⊗	⊗	⊗	⊕	⊕	⊕	⊕	⊗	⊕	⊗
Chiapasco et al. [51]	⊕	⊕	⊕	⊗	⊗	⊗	⊕	⊕	⊕	⊕	⊗	⊕	⊕
Chiapasco et al. [17]	⊖	⊕	⊖	⊗	⊗	⊗	⊕	⊕	⊕	⊕	⊕	⊕	⊗
Chiapasco et al. [50]	⊖	⊕	⊖	⊕	⊗	⊗	⊕	⊕	⊕	⊕	⊕	⊕	⊕
Fang et al. [47]	⊖	⊕	⊖	⊗	⊗	⊗	⊕	⊕	⊕	⊕	⊕	⊕	⊗
Wang et al. [48]	⊕	⊕	⊕	⊗	⊕	⊕	⊕	⊕	⊗	⊕	⊕	⊕	⊕
Ariga et al. [52]	⊖	⊕	⊖	⊗	⊗	⊗	⊕	⊕	⊗	⊕	⊕	⊖	⊗
Attia et al. [45]	⊖	⊕	⊖	⊗	⊗	⊗	⊕	⊕	⊕	⊕	⊗	⊕	⊗
Pellegrino et al. [49]	⊖	⊕	⊖	⊕	⊗	⊗	⊕	⊕	⊕	⊕	⊕	⊕	⊕

Figure 2B. Quality assessment and risk of bias summary.

Study characteristics

The included studies of the present systematic review consisted of three prospective studies, six retrospective studies, and one randomized clinical trial as described in Table 3. Five studies were conducted in Europe [17,45,49-51], one in the USA [3], and four in Asia [15,47,48,52]. The present review pooled data obtained from 242 patients (167 males and 75 females), with the age range of 13 to 79 years of age as shown in Table 3. A total of 848 dental implants were placed in the free fibula flaps. All dental implants were placed in a delayed fashion, ranging from 14 to 192 months. The mean follow-up period ranged from 1 to 11.67 years. Out of 848 dental implants, 793 implants successfully osseointegrated and 55 implants failed. The success rate ranged from 85.5% to 98.6% reported in 6 studies [17,45,47-49]. The success of all dental implants in the included studies was evaluated according to the

criteria proposed Albrektsson et al. [46] for implant success.

Meta-analysis

Figure 3A shows the statistical analysis results regarding the success proportion of the implants across the studies demonstrated in a forest plot. The proportion of successful implants and the success rate of the implants placed in fibula were pooled from the results across 10 articles using a random effect model [3,15,17,45,47-52]. The estimated proportion of successful implants in fibula was 0.94 or 94% (95% CI = 0.91 to 0.96) with an insignificant heterogeneity of 37%, P = 0.12.

Figure 3B shows the failure rate of the implants placed in the fibula. Using a random effect model the annual implant failure rate was 0.02 with 95% CI = 0.01 to 0.03. The heterogeneity was 74% for I² and significant with a P < 0.01.

Table 3. General characteristics of included studies

Study	Year of publication	Type of study	Number of patients	Age of patients (years)	Gender		Number of implants	Number of implants		Type of pathology			Criteria for outcome measure
					M	F		Success	Failed	Malignant	Benign	Trauma	
Roumanas et al. [3]	1997	Prospective	14	25 - 78	7	7	49	47	2	13	-	1	Yes
Chiapasco et al. [17]	2006	Prospective	16	13 - 66	12	4	71	66	5	9	7	-	Yes
Attia et al. [45]	2018	Retrospective	34	17 - 79	23	11	134	122	12	27	7	-	Yes
Fang et al. [47]	2015	Retrospective	74	19 - 75	61	13	192	174	18	47	9	18	Yes
Wang et al. [48]	2015	Retrospective	19	28 - 55	12	7	51	44	7	-	19	-	Yes
Pellegrino et al. [49]	2018	Retrospective	21	49.6	15	6	108	106	2	15	6	-	Yes
Chiapasco et al. [50]	2011	Retrospective	12	51 - 68	1	11	75	72	3	-	12	-	Yes
Chiapasco et al. [51]	2000	Prospective	8	23 - 60	5	3	31	30	1	6	2	-	Yes
Ariga et al. [52]	2017	Retrospective	10	18 - 59	5	5	33	31	2	-	10	-	Yes
Kumar et al. [53]	2016	Randomized clinical study	34	33.95	26	8	104	101	3	10	24	-	Yes

M = male; F = female.

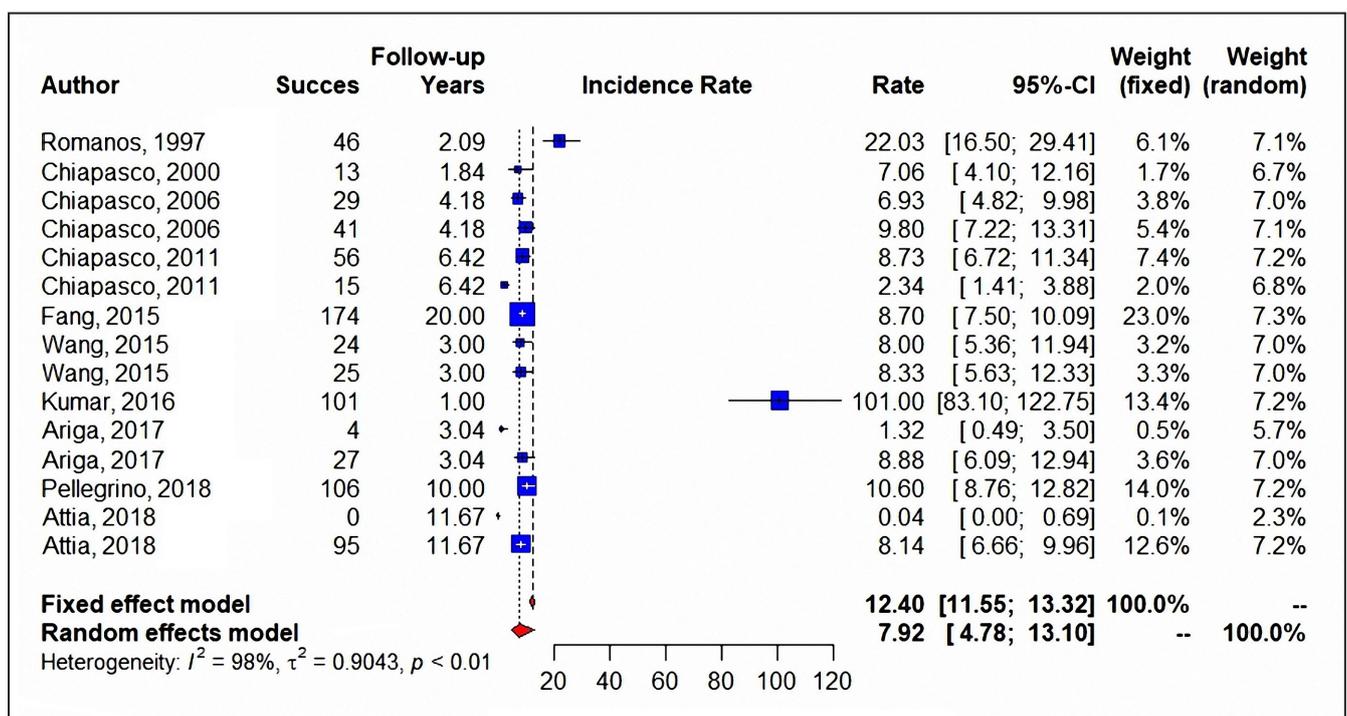


Figure 3A. Forest plot shows the proportion of successful implants placed in the fibula.

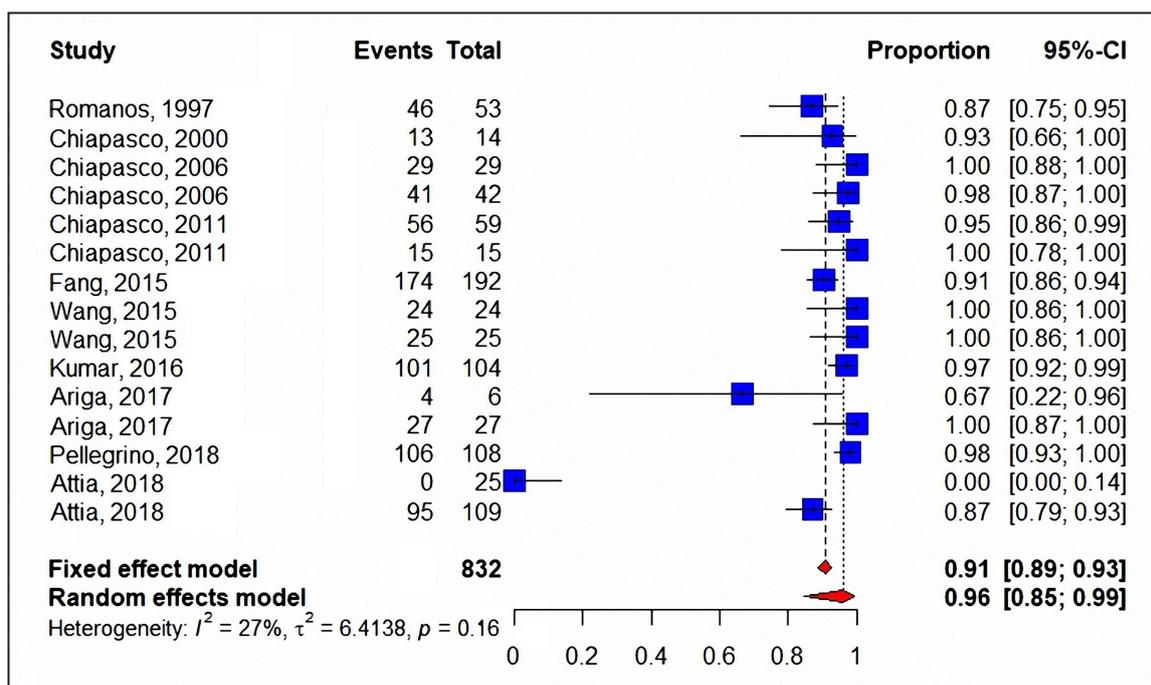


Figure 3B. Forest plot shows the failure rate of the implants placed in the fibula.

DISCUSSION

The main purpose of this study is to provide a systematic review and meta-analysis on the success of dental implants placed secondarily in free fibula flaps following reconstruction of maxillary and mandibular continuity defects, using the Albrektsson et al. [46] criteria for measuring the success. The criteria of Albrektsson et al. [46] evaluates all aspects related to implant success, including implant stability, peri-implant bone loss after the first year of use, peri-implant hard and soft tissue health, and patient-related factors including pain and infection or any other symptoms that would affect the success of the implants.

The findings of this systematic review and meta-analysis support that: dental implants placed secondarily in free fibula flaps can successfully osseointegrate and be used for dental rehabilitation. The use of vascularized fibula is a reliable method for reconstructing long continuity defects with full prosthetic dental rehabilitation after implant placement. The results of this review in regards to the success of dental implants placed in the fibula are consistent with other studies that measured this outcome [26,27,31,33,36], but did not use an objective measure of success. Ferrari et al. [33] evaluated the clinical outcome and aesthetic and functional results of implants inserted and prosthetically restored in free fibula flaps. The authors reported 91.9% survival rates of 62 implants followed over 10 years. Wu et al. [27]

also reported the clinical outcome of implants placed in the fibula flaps; the study reported high implant stability placed in fibula, 96% and 91% at 1 year and 5-year cumulative survival rate respectively, and 95%, 87 % at 1 year and 5-year cumulative success rate respectively. A prospective study by Kramer et al. [26] in 2005 evaluated the efficacy of dental implants placed in fibula using resonance frequency analysis and reported a success rate of 96.1 % over an average period of 2.5 years.

Bone grafting of significant continuity defects can be quite challenging due to the risk of resorption, exposure, infection, and ultimately loss of the graft. The two proposed options for reconstruction are vascularized free tissue transfer or non-vascularized bone grafts, including autogenous, allografts, xenografts, and synthetic grafts. The former is harvested from a donor site with its blood supply. The choice of bone grafts should be guided by the size and type of the defect, type of tissues lost that requires replacement, need for adjunct therapy (i.e., radiotherapy), and host overall health [30,50,51].

Pogrel et al. [56] in 1997 compared vascularized versus non-vascularized flaps following segmental defects of the mandible. The study showed a direct correlation between the size of the defect and the type of graft. The authors reported higher success with vascularized flaps vs. non-vascularized flaps for reconstruction of continuity defects exceeding 9 cm. Chiapasco et al. [51] in 2000, compared bone resorption of autogenous bone grafts versus vascularized free flaps. Vascularized bone flaps

showed less bone resorption before implant insertion and loading and showed no difference in peri-implant bone resorption after insertion and loading. Since vascularized bone flaps are transferred with their own blood supply tissues, they do not undergo resorption/remodelling and thus maintain original volumes. This is a significant advantage of vascularized bone flaps, especially when the time of the implant placement and prosthetic loading cannot be determined or will take place after a period of time following reconstruction, for example, in patients undergoing radiotherapy. Another important consideration is the timing of implant placement in free bone flaps. Implants can be placed immediately at the time of reconstruction or secondarily, months after the initial procedure. For non-vascularized bone grafts, delayed implant placement, usually 4 to 6 months after initial reconstruction, is essential to allow for bone healing and consolidation. Vascularized tissues, on the other hand, do not require a consolidation period and are not subject to volume changes, so immediate placement of implants can be done [47,48,51]. Appropriate angulation and implant alignment can be challenging without pre-operative planning. Ideally virtual surgical planning should be utilized, especially when done immediately. In addition, if the occlusion and opposing dentition are not used for guidance at the time of immediate implant placement, dental rehabilitation, later on, may not be feasible [48,51,52]. Additional considerations that may negatively impact the success of dental implants placed immediately is the need for adjunct therapy, specifically radiotherapy [30]. Finally, immediate implant placement adds surgical time, ischemia time (if the implants are not placed in situ) which in turn may impact flap survival and pose a risk for direct injury to the vessel pedicle. To the best of our knowledge, this is the first systematic review and meta-analysis undertaken to evaluate the success of osseointegrated dental

implants placed secondarily in the fibula flaps. The main strength of this systematic review and meta-analysis is that it only included studies that used the Albrektsson and colleagues criteria to evaluate implant success [46]. The following criteria evaluates all aspects related to implant success, stability, bone loss, hard and soft tissue health, and patient-related factors, thus making it the most objective and comprehensive implant success evaluation tool. The main limitation of our study is the limited number of articles that met the inclusion criteria and the fact that some of the articles used a convenient sample with a moderate to high risk of bias. Furthermore, the included studies didn't have adequate data pertaining to the radiation therapy received and its effects on the dental implants.

CONCLUSIONS

The results of this systematic review and meta-analysis strongly indicate that using objective criteria, delayed implant placement in free fibula flaps is highly successful. These osseointegrated implants can be used for dental rehabilitation allowing for restoration of form and function, which is the ultimate goal. Further prospective studies are needed to better evaluate long-term outcomes of implant placement in free osseous flaps, using objective tools such as the Albrektsson and colleagues proposed criteria [46].

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