



# Factors affecting anastomosis failure in microvascular fibula flap reconstruction of the maxillofacial region: a systematic review and meta-analysis

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**Abstract** (J Korean Assoc Oral Maxillofac Surg 2025;51:3-16)

This systematic review and meta-analysis evaluates the contributory factors and failure rates in anastomosis during microvascular fibula flap reconstruction in maxillomandibular regions. A comprehensive search strategy was employed across databases including MEDLINE, Web of Science, EMBASE, Scopus, Cochrane's CENTRAL, as well as grey literature sources, and manual searches of noteworthy journals, covering studies from inception up to April 2023. The inclusion criteria targeted retrospective or prospective cohort and clinical studies that investigated functional and dental rehabilitation outcomes in human subjects undergoing maxillofacial reconstruction using microvascular fibula flaps. Exclusion criteria encompassed case-control studies, alternative reconstruction method research, and animal-based investigations. The study's findings revealed a cumulative vascular failure rate of 6%. Subsequent analysis delineated the primary causes of this failure, attributing 3% to venous thrombosis, 1% to arterial thrombosis, and less than 1% to blood vessel compression due to hematoma. However, notable heterogeneity across the studies indicates substantial variability in vascular failure rates reported. These results of our review and meta-analysis underscore the intricate factors impacting anastomosis success, such as anastomosis technique, recipient vessel quality, the choice between couplers.

**Key words:** Surgical anastomosis, Fibula, Treatment outcome

[paper submitted 2023. 6. 28 / revised 2023. 11. 12 / accepted 2023. 11. 20]

## I. Introduction

Maxillofacial defects that result from congenital abnormalities, traumatic injuries, or the surgical removal of tumors pose significant challenges for both patients and healthcare providers. These defects disrupt essential functions such as mastication, speech, and swallowing, and they also significantly affect patients' psychosocial well-being and overall quality of life<sup>1,2</sup>. In recent years, various reconstructive techniques

have emerged to address these challenges, and microvascular fibula flap (FFF) reconstruction stands out for its potential for successful osseointegration<sup>3</sup>.

Despite significant advances in reconstructive techniques, the intricacy of FFF reconstruction procedures and patient-specific factors can occasionally result in failures<sup>4</sup>. A critical component of these procedures is the anastomosis, or surgical connection, of separate or severed vessels, which can be categorized broadly into venous and arterial anastomosis, each with its own unique set of challenges and considerations<sup>5</sup>.

Venous anastomosis, which connects the vein of the free flap to a vein in the recipient site, is pivotal in ensuring the success of the procedure. As an essential aspect of postoperative flap survival, venous anastomosis allows the outflow of blood from the flap, preventing a buildup of blood that could lead to venous congestion. Failures primarily occur due to flap congestion, often secondary to venous thrombosis. Thrombosis is a significant concern because it can lead to

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vessel blockage, thereby compromising the viability of the flap. This problem is often exacerbated by patient-specific factors such as underlying coagulation disorders or systemic conditions that affect vascular health<sup>6</sup>.

In contrast, arterial anastomosis involves connecting the artery in the free flap to an artery in the recipient site, providing an inflow of blood to the flap. Although arterial thrombosis is less common than venous thrombosis, it remains a serious potential complication. Failures in arterial anastomosis can lead to insufficient perfusion to the flap, potentially resulting in tissue necrosis. This situation is often influenced by the caliber and condition of the recipient vessels, so careful selection and preparation of the recipient site is necessary<sup>7</sup>.

Beyond venous and arterial anastomosis, other factors can contribute to the failure of FFF reconstruction. For example, postoperative hematoma can lead to vascular compression, which can in turn compromise blood flow and lead to flap failure. Similarly, wound dehiscence, the separation of the wound edges, can put tension on the anastomotic site, possibly leading to vessel thrombosis or tearing<sup>8,9</sup>.

Various strategies and methods have been proposed to mitigate these complications, such as the use of venous coupler devices instead of hand-sewn sutures. These devices, which were introduced in the 1960s, can simplify the anastomosis process, potentially reducing the time the tissue is without a blood supply and thus lowering the risk of thrombosis<sup>7</sup>. However, although preliminary results from retrospective studies are promising, these interventions need further validation through robust, prospective research to ensure their effectiveness and safety<sup>10,11</sup>. In that context, our systematic review and meta-analysis evaluates the failure rate and identifies factors that affect anastomosis in FFF reconstruction. We critically analyze the available literature, including randomized controlled trials (RCTs), cohort studies, and case series, to gather comprehensive evidence about the vascular complications and determinants of success in FFF reconstruction.

## II. Materials and Methods

This systematic review and meta-analysis was meticulously designed and executed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines and the Cochrane Handbook for Systematic Reviews of Interventions to ensure a comprehensive and rigorous investigation<sup>12</sup>.

### 1. Research question formulation

We developed well-structured research question based on the PICO framework, as follows:

- Population: Patients undergoing maxillofacial reconstruction using microvascular fibula flaps.
- Intervention: Implementation of arterial and venous anastomosis.
- Comparison: Comparison of anastomosis techniques, such as couplers, and the use of different arteries and veins for anastomosis.
- Outcome: Failure rates pertinent to vascular compromise and its underlying causes.

### 2. Literature search strategy

We performed an exhaustive, multi-platform literature search in the MEDLINE, Web of Science, Embase, Scopus, and Cochrane's CENTRAL databases from the inception of each source to April 2023. We further probed the gray literature, encompassing trial registrations, conference proceedings, dissertations, and other non-peer-reviewed sources, to ensure a holistic approach. Specific search terms were tailored for each database and included "maxillofacial reconstruction" and "fibula flap." High impact factor (>1) journals specializing in maxillofacial reconstruction were also scrutinized manually. A comprehensive tabulation of our search strategies and results is provided in Table 1.

### 3. Inclusion and exclusion criteria

Our stringent selection criteria targeted studies with retrospective or prospective cohort and clinical designs and human subjects that focused on graft anastomosis in microvascular fibula flap maxillofacial reconstructions. We excluded case-control studies, research involving other types of reconstruction methods, and animal-based studies.

### 4. Study selection process

Two independent authors (H.M. and S.S.) screened the titles and abstracts of potentially relevant articles according to the PICO framework and the predetermined inclusion and exclusion criteria. Any disagreements were resolved by consulting a third author (R.T.). A comprehensive full-text review of the selected articles ensured strict adherence to the research criteria, with rationales documented for excluded studies.

**Table 1.** Custom search strategy for each database

Database	Search strategy used	Hits
MEDLINE via PubMed	(microvascular OR composite flap OR microvascular transplant) AND (fibula) AND (maxillofacial OR oral cavity)	395
Web of Science core collection	((ALL=(microvascular OR composite)) AND ALL=(fibula)) AND TS=(oral OR maxillofacial OR mandib? OR maxill?)	353
Embase	#1 'microvascularization'/exp OR 'microvascularization' OR 'composite flap'/exp OR 'composite flap' 3,768 #2 ('fibula'/exp OR 'fibula' OR fibular) 24,239 #3 'mouth cavity'/exp OR 'mouth cavity' OR 'maxillofacial injury'/exp OR 'maxillofacial injury' 109,794 #4 #1 AND #2 AND #3	26
Scopus	ALL (microvascular OR composite) AND TITLE-ABS-KEY (fibula) AND TITLE-ABS-KEY (maxillofacial AND injury OR maxillofacial AND trauma OR maxillofacial AND reconstruction)	287
Cochrane central register of controlled trials	#1 microvascular anastomosis 62 #2 microvascular 4,444 #3 fibular 326 #4 maxillofacial 5,248 #5 oral 239,600 #6 (#1 OR #2) AND #3 AND (#4 OR #5) 4	4
Total		1,065

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## 5. Data extraction and management

One researcher (R.T.) meticulously extracted pertinent data from the selected articles, and that work was cross-verified by another researcher (S.S.). We collected the study details, patient demographics, clinical presentation, anastomosis techniques, assessment methods, and outcome measures, among other data points. This information was systematically catalogued using piloted data extraction forms. A comprehensive summary of the extracted data is presented in Table 2.

## 6. Risk of bias assessment

To ensure the credibility of our findings, we assessed the risk of bias in the included studies. For the retrospective and prospective cohort studies, we used the Newcastle–Ottawa scale to evaluate the quality of their selection, comparability, and outcomes. For RCTs, we used the Cochrane's risk of bias tool. The risk of bias assessment results are presented in Table 3.

## 7. Data synthesis and analysis

For the data to be suitable for a meta-analysis, we had to ensure the comparability of the therapeutic interventions and measured outcomes across studies. The overall failure rates caused by vascular compromise and specific failures were pooled by calculating standard errors for each study with

consideration of the failure rate and the study size. Inverse-variance random-effects meta-analyses were conducted for all of the aforementioned outcomes. We found several sources of heterogeneity: differences in treatment, treated populations, study design, and data analysis methods. In the absence of heterogeneity, estimates are considered to differ only due to random sampling errors. Heterogeneity is important, and investigating sources of heterogeneity in meta-analyses involves the identification of study-level characteristics associated with differences in outcomes. Methods commonly used to do that are subgroup analyses and meta-regressions.

Heterogeneity between studies was tested using Cochrane's Q test and quantified using  $I^2$  statistics, which measure the inconsistency in pooled calculations caused by study heterogeneity. The pooled failure rates were computed using STATA 17 (Stata Corp.). We want to provide accurate and reliable information, so we take concerns about heterogeneity in the results seriously, particularly the incidence and causes of vascular insufficiency across studies. Although it is true that heterogeneity can cause variability in pooled estimates, we have made every effort to analyze and interpret the available data with care. Additionally, we relied on established scientific methods to account for heterogeneity, such as performing subgroup analyses and using random effects models.

**Table 2.** Summary of studies included in the review

Study	Study design	No. of subjects	Sex of subjects	Duration of the study	Defect location	Anastomosis (arteries)	Anastomosis (veins)	Assessments	Comorbidities	Indications for surgery	No. of grafts	No. of graft failures due to blood vessels	Reasons for vascular failure
Abramowicz et al. <sup>17</sup> (2021)	Retrospective	15	10 M, 5 F	2010 to 2020	Mandible	Facial (n=13), superior thyroid (n=1), transverse cervical (n=1)	External jugular (n=9), common facial (n=5), anterior jugular (n=1)	Postoperative course, complications, tumor recurrence Doppler device was used to detect the perforators of the skin paddle to check if the blood supply was adequate	NS	Mandibular tumor	15	No failures	N/A
Aksöylek et al. <sup>18</sup> (2021)	Retrospective	120	100 M, 20 F	1992 to 2018	Mandible	Both vein and artery: 100, lingual 50, external jugular and facial 24, facial 12, external jugular and lingual 6, lingual and facial 4, internal jugular and facial 4	Single veins: 348, external jugular 184, facial 72, internal jugular 48, supra-parathyroid 26, lingual 18. Double veins: 406, external jugular and internal jugular 188, facial and external jugular 138, lingual and external jugular 32, supra-thyroid and external jugular 24, facial and supra-thyroid 14, supra-thyroid and internal jugular 8, lingual and internal jugular 2	Doppler device was used to detect the perforators of the skin paddle to check if the blood supply was adequate	NS	Squamous cell carcinoma of the oral cavity, mandible (n=10), and osteoradionecrosis of the mandible (n=2). Not explicitly provided; however, defects in the head and neck region is mentioned	120	24	Thrombosis (A4, V4, A & V5, hematoma compression 1, kinking due to acute angle between the fibula axis and the pedicle 11)
Assoumane et al. <sup>19</sup> (2017)	Retrospective	601	417 M, 184 F	July 2013 to December 2015	Tongue, mandible, buccal mucosa, mandible/gingiva, floor of mouth, retromolar region, pharynx, hard or soft palate, maxilla, infraorbital zygoma, parotid region, neck	Both vein and artery: 100, lingual 50, external jugular and facial 24, facial 12, external jugular and lingual 6, lingual and facial 4, internal jugular and facial 4	Single veins: 348, external jugular 184, facial 72, internal jugular 48, supra-parathyroid 26, lingual 18. Double veins: 406, external jugular and internal jugular 188, facial and external jugular 138, lingual and external jugular 32, supra-thyroid and external jugular 24, facial and supra-thyroid 14, supra-thyroid and internal jugular 8, lingual and internal jugular 2	Clinical observation, external Doppler examination	Not provided in the manuscript	Not explicitly provided; however, defects in the head and neck region is mentioned	854	862 for hand sewn, 8/519 for couplers	Dehiscence in hand sewn, thrombosis in couplers
Gaegel et al. <sup>15</sup> (2009)	Retrospective	9	5 M, 4 F	NS	Maxilla or severe alveolar ridge deficiency of the mandible	Facial artery, labial superior artery	Facial vein, angular vein	Preoperative panoramic radiograph and CT, intraoperative Doppler ultrasound of facial and labial arteries, postoperative Cook-Swartz Doppler flow probe, postoperative panoramic radiographs, and dental CT scan	Two patients had undergone irradiation of the local bone and the neck region more than one year before reconstruction. These patients had previous unsuccessful free iliac crest transplants	Trauma, severe atrophy, resection of tumor, or partial loss of the premaxilla in a cleft lip, palate, and alveolar patient	6 microvascular corticoosseous flaps, 2 microvascular osseous fibula flap	No failures	No failures
González-García et al. <sup>16</sup> (2008)	Retrospective	102, 42 of whom reconstruction of mandibular defects by means of a vascularized free fibular flap.	70 M, 32 F	5 years (1996 to 2001)	Oral and maxillofacial defects, mandibular defects	Superior thyroid artery	Truncus thyrofacialis, external jugular vein system	Aesthetic and functional results (evaluated in categories: excellent, good, or poor)	NS	Benign (n=15) and malignant (n=27) conditions. The most frequent entity was squamous cell carcinoma of the oral cavity (n=26)	42 vascularized free fibular flaps were used	5	Thrombosis (V2), hematoma, compression 3
Han et al. <sup>17</sup> (2013)	Retrospective	201	109 M, 92 F	January 2005 to April 2012	Mandibular defects	Superior thyroid, facial, lingual	Internal jugular vein, external jugular vein, anterior jugular vein, common facial vein	Clinical examinations, color Doppler ultrasound examination of the calf, portable Doppler used on the tenth day after surgery	NS	Malignant tumors, osteoradionecrosis, odontogenic keratocyst, carcinoma of the oral cavity (n=26)	201	6 vascular thrombosis (single 3/112, dual 3/89)	Thrombosis, twisted or kinked vascular pedicle
Johal et al. <sup>18</sup> (2022)	Retrospective	83	81 M, 2 F	2004 to 2020	Head and neck	NS	The donor vein graft was sourced from the lower limb in 79 cases, the local neck in 3 patients, and the upper limb in a single case	NS	NS	More than 3,000 free flaps were performed for head and neck reconstruction (oral cancer), 124 soft tissue reconstructions to the lower limb and other miscellaneous cases, including pediatric surgery	116 vein grafts in total in 33 of the 83 patients, sequential (two) vein grafts were used, with a single vein graft used in the remaining 50 cases	683 cases experienced flap loss	Not specified
Li et al. <sup>10</sup> (2015)	Retrospective	69	31 M, 38 F	December 2012 to December 2014	Mandible	Facial artery, superior thyroid artery, lingual artery	Internal jugular vein, facial vein, external jugular vein	Postoperative vascular patency, thrombosis, and flap survival were assessed by monitoring the clinical manifestations of the flaps. Complications such as venous congestion and arterial insufficiency were verified by a decreased arterial or venous Doppler signal	11 had a history of hypertension, 3 had diabetes mellitus, 3 had a history of radiation therapy, and 1 had hepatitis C	The most common reason for surgical defects was tumor (34 malignant tumors), 1 benign tumor, 4 other cases had defects caused by trauma (1 case), osteomyelitis (1 case), and osteoradionecrosis (2 cases)	69 simultaneous free flap procedures	These flaps (4.55%) developed venous thrombosis	Thrombosis (V3) and venous hemorrhage

Table 2. Continued

Study	Study design	No. of subjects	Sex of subjects	Duration of the study	Defect location	Anastomosis (arteries)	Anastomosis (veins)	Assessments	Comorbidities	Indications for surgery	No. of grafts	No. of graft failures due to blood vessels	Reasons for vascular failure
Mücke et al. <sup>24</sup> (2014)	Prospective	196	NS	September 2008 to January 2010	Mandible, tongue, maxilla, and cheek	External carotid artery	NS	Blood flow, velocity, hemoglobin concentration, and oxygen saturation measurements were taken preoperatively at the donor site and on the flap on the first, second, and seventh postoperative day and after 4 weeks	Not specified.	Oral cavity reconstruction after oncological operations	196	10/196	NS
Seethil Mungai et al. <sup>25</sup> (2018)	RCT	124	73 M, 51 F	January 2010 to December 2016	Maxillofacial region	NS	Group A patients underwent a microvascular coupler device (Synovis Life Technologies Inc.). In group B patients, the venous anastomosis was performed using conventional hand-sewn sutures (8-0 Prolene)	Intraoperatively, the time taken to complete the anastomosis and leakage from the vessels were recorded. The incidence of venous thrombosis was assessed by checking the flap color	None	Surgery for primary or secondary reconstruction in patients with maxillofacial defects due to benign tumors	124 fibula free flaps	4 (three in the same group due to thrombosis, and one in the coupler group due to extension of the coupler device after infection)	Thrombosis in the suture group, and extension of the coupler device after infection in the coupler group
Pohlman et al. <sup>19</sup> (2007)	Retrospective	532	297 M, 235 F	1987 to 2005	Head and neck region	NS	NS	Review of medical records and analysis of the primary tumor site, flap type, outcome, and complications	NS	Malignant neoplasm	540	34 total flap losses (6.2%) occurred. 7 were due to vascular problems	Thrombosis of one of the vessels (8.6% arterial, 6.6% venous) and major bleeding (6.3%) were the most frequent causes of failure in microvascular free tissue transfer
Rischl et al. <sup>20</sup> (2022)	Retrospective	23	NS	January 2013 to 2020	Mandibular	NS	NS	CT angiography, handheld Doppler (HandyDop <sup>®</sup> )	NS	Mandibular reconstruction	NS	No failures	No failures
Rosenblat et al. <sup>21</sup> (2004)	Retrospective	117	89 M, 28 F	August 2001 to October 2002	Head and neck	Facial artery	NS	Preoperative evaluation by physical examination and/or lower extremity Doppler ultrasonography and postoperative monitoring with color Doppler and temperature checks	NS	Head and neck defects (specifically 11 midface, 41 composite, 35 oral cavity, 17 hypopharyngeal, and 20 cutaneous defects)	125	5	Arterial insufficiency (in four flaps), venous insufficiency (in one flap)
Schantz et al. <sup>22</sup> (2017)	Retrospective	46	26 M, 20 F	September 2010 to August 2012, with a follow-up time of 13.72 months (SD 6.11)	Mandible (in 45 patients) and maxilla (in 1 patient)	NS	NS	Muscle function, sensitivity, pain on palpation, deformities, scarring, persisting pain, and gait pattern	NS	Deep-circumflex iliac artery 27 patients, fibula 19 patients	NS	NS	NS
Vermie-Mosca et al. <sup>23</sup> (2020)	Retrospective	46	38 M, 8 F	January 1, 2010 to December 31, 2017	Oral floor (30.4%), oropharynx (28.3%), hypopharynx (17.4%), lingual margin (13%), larynx and ethmoid (2.2% each)	Superior thyroid artery (37.3%) and facial artery (33.3%)	Facial vein (18.5%), thyro-linguo-facial trunk (18.5%), external jugular vein (16.7%)	Not mentioned.	76% of patients had active tobacco use, and 60.8% had active alcohol use	Excision of carcinoma (all patients had squamous cell carcinoma, except for one who had an adenocarcinoma)	51 grafts were performed for 46 patients (2 grafts were needed for 5 of the patients)	8 patients experienced vascular distress (15.7%)	Majority of vein thrombosis (6 vein thrombosis out of 8 total), primarily the internal jugular veins (n=3) and anterior jugular veins (n=2). Two thromboses occurred after coupler anastomosis and 4 after manual anastomosis. The arteries that thrombosed in both cases were the superior thyroid arteries

(M: male, F: female, NS: not specified, N/A: not applicable, CT: computed tomography, RCT: randomized controlled trial, SD: standard deviation)  
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**Table 3.** The risk of bias in the included studies based on the Newcastle–Ottawa scale

Newcastle–Ottawa criteria	Study													
	Abramowicz et al. <sup>13</sup> (2021)	Aksoyler et al. <sup>14</sup> (2021)	Assoumane et al. <sup>11</sup> (2017)	Gaggi et al. <sup>15</sup> (2009)	González-García et al. <sup>16</sup> (2008)	Han et al. <sup>17</sup> (2013)	Johal et al. <sup>18</sup> (2022)	Li et al. <sup>10</sup> (2015)	Mütcke et al. <sup>24</sup> (2014)	Pohlentz et al. <sup>19</sup> (2007)	Ritschl et al. <sup>20</sup> (2022)	Rosenthal et al. <sup>21</sup> (2004)	Schardt et al. <sup>22</sup> (2017)	Vernier-Mosca et al. <sup>23</sup> (2020)
<b>A. Selection (maximum of four stars)</b>														
1. Representativeness of the exposed cohort	★	★	★	★	★	★	★	★	★	★	★	★	★	★
2. Selection of the non-exposed cohort	☆	☆	☆	☆	★	★	☆	★	★	★	★	☆	★	★
3. Ascertainment of exposure	★	★	★	★	☆	★	★	★	★	☆	★	★	★	★
4. Demonstration that outcome of interest was not present at start of study	★	★	★	★	★	★	★	★	★	★	★	★	★	★
<b>B. Comparability (maximum of two stars)</b>														
1. Comparability of cohort on the basis of the design or analysis	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆	☆☆
<b>C. Outcome (maximum of three stars)</b>														
1. Assessment of outcome	★	★	★	★	★	★	★	★	★	★	★	★	★	★
2. Was follow-up long enough for outcomes to occur?	★	★	★	★	★	☆	★	☆	★	★	☆	★	☆	★
3. Adequacy of follow-up of cohorts	★	★	★	★	★	★	★	★	★	★	★	★	★	★
Total (maximum of nine stars)	6	6	6	6	7	7	6	7	9	7	7	5	7	9

Senthil Murugan et al.<sup>25</sup> (2018) – Randomization process: some concerns, Deviations from intended interventions: some concerns, Missing outcome data: low, Measurement of the outcome: low, Selection of the reported result: some concerns, Overall bias: some concerns.

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### III. Results

#### 1. Screening and selecting studies

The initial search strategy yielded 769 unique articles. Following a preliminary assessment of titles and abstracts, 738 were ruled out due to their lack of relevance, leaving 31 for further evaluation. An additional four studies were identified through our scrutiny of the gray literature, and six were found through citation searches. Those 40 full-text articles (10 found by hand and 30 through digital searches) were screened according to the inclusion and exclusion criteria. After that, 15 studies were included, and 25 studies were excluded. The process of study identification, inclusion, and exclusion, along with the reasoning behind each decision, is comprehensively illustrated in Fig. 1.

#### 2. Descriptive analysis of studies

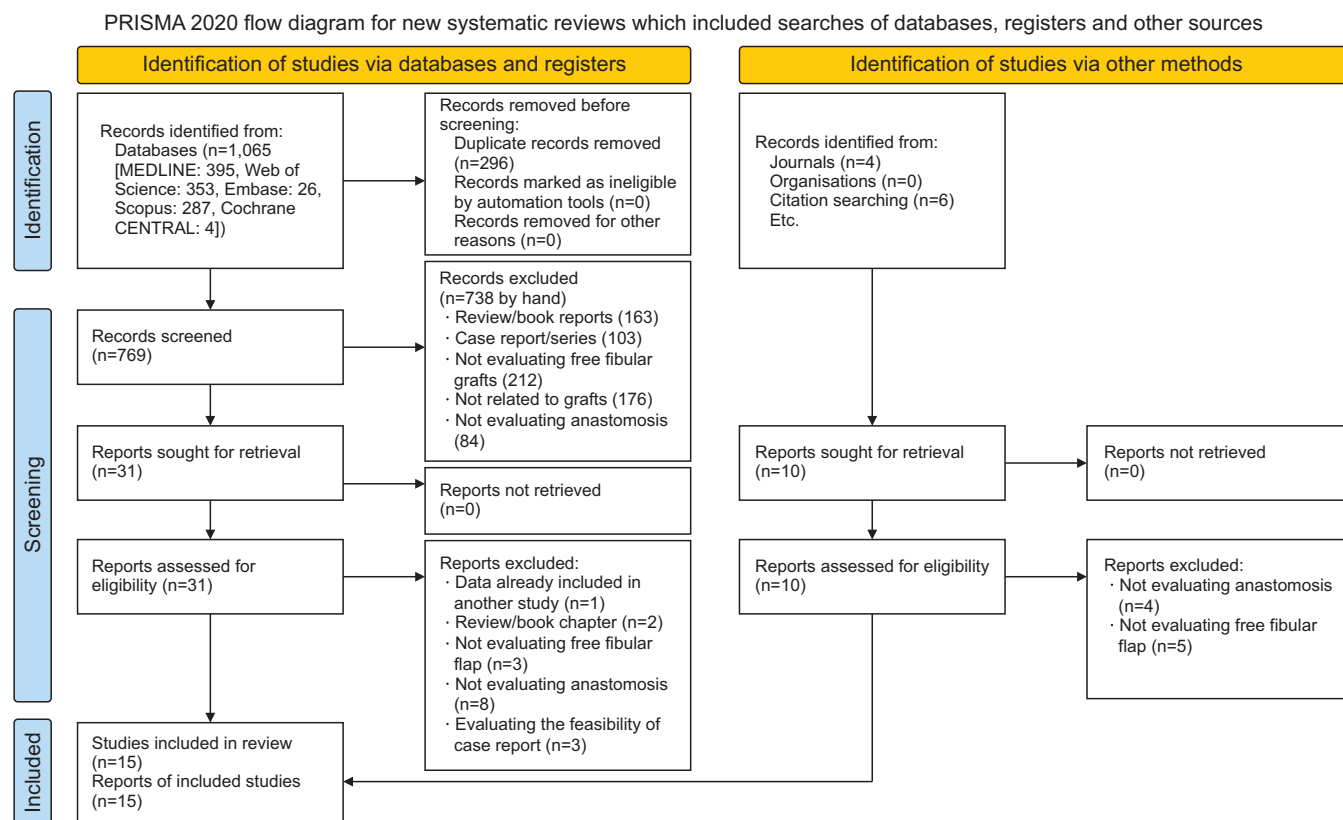
This systematic review comprises 15 studies: 13 retrospective cohort studies<sup>10,11,13-23</sup>, one prospective cohort study<sup>24</sup>, and

one randomized clinical trial<sup>25</sup>. The studies were conducted from 2007 through 2022 and collectively included 2,284 patients, 1,346 males, 719 females, and 219 whose sex was not reported. The sample sizes across studies were diverse, ranging from a minimum of nine in Gaggl et al.<sup>15</sup> to a maximum of 601 in Assoumane et al.<sup>11</sup>, with a higher prevalence of male subjects in all the studies.

The duration of the studies also varied considerably, with Abramowicz et al.<sup>13</sup> reporting the longest duration of ten years. Defect locations were primarily in the head and neck regions, with a particular focus on mandibular defects, but they also extended to other regions such as the oral floor and oropharynx.

The anastomoses encompassed the facial, superior thyroid, and lingual arteries and the external jugular, common facial, and anterior jugular veins. The assessment methodologies ranged from Doppler devices to clinical observation and radiographs.

The number of grafts performed varied from study to study, with a minimum of six in Gaggl et al.<sup>15</sup> and a maximum of 854 in Assoumane et al.<sup>11</sup>. Vascular complications led to



**Fig. 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 flow diagram. Adapted from the article of Page et al.<sup>12</sup> (BMJ 2021;372:n71) under the terms of the Creative Commons Attribution (CC BY 4.0) license.

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graft failures in several studies, with common causes including thrombosis, hematoma compression, dehiscence, and a twisted or kinked vascular pedicle. Some studies reported no instances of failure (Abramowicz et al.<sup>13</sup>, Ritschl et al.<sup>20</sup>). A detailed representation of these characteristics is provided in Table 2.

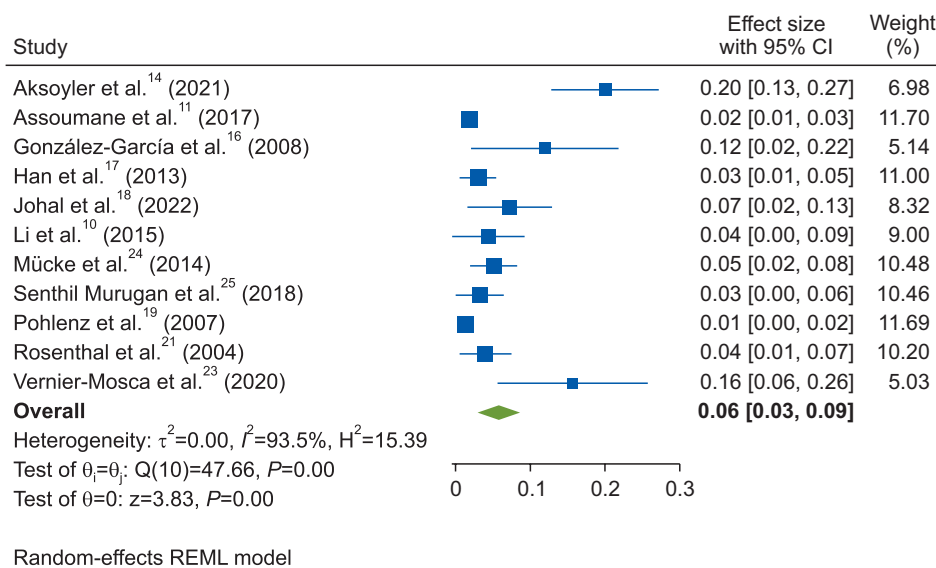
### 3. Assessment of bias

The risk of bias in the 13 retrospective and one prospective cohort study ranged from low to high on the Newcastle–Ottawa scale (scores 5 to 9). Senthil Murugan et al.’s RCT<sup>25</sup> also had some bias-related concerns. Therefore, the interpretation of our results must take into account the diverse methodological quality of the included studies. Detailed risk of bias assessments for all studies are presented in Table 3.

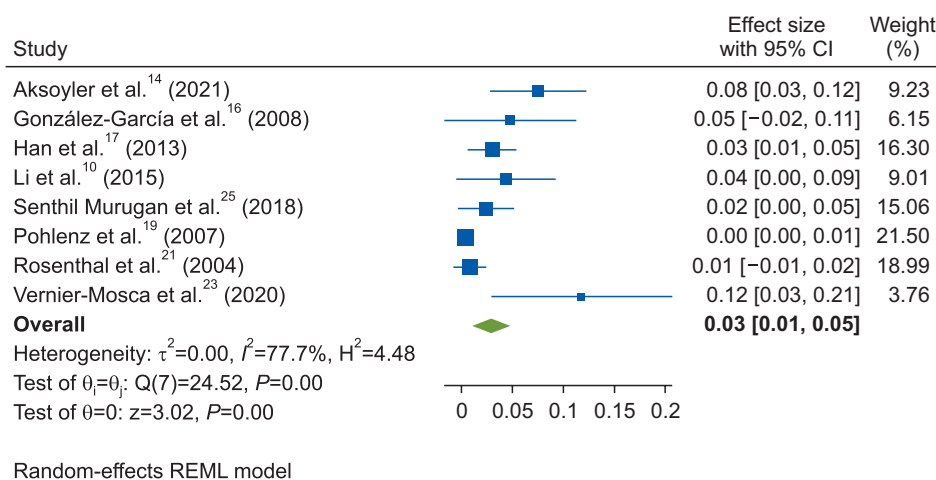
### 4. Synthesis of data and meta-analysis

Despite the diverse set of studies, we constructed a meta-analysis to find overarching trends in vascular-related failures and discern the primary etiologies of those failures. Unfortunately, given the considerable variation in intervention strategies and outcome measures across studies, it was unfeasible to conduct a meta-analysis comparing different host veins and arteries, double versus single anastomoses, and the use of couplers versus hand suturing techniques.

To ascertain the overall rate of vascular failure, we pooled data from 11 studies that collectively account for 2,405 free fibula grafts. The pooled vascular failure rate was approximately 6% (confidence interval [CI] 0.03-0.09). However, that estimate should be interpreted with caution because the underlying heterogeneity was quite high ( $I^2=93.5%$ ), indicative of significant variability across the contributing studies.



**Fig. 2.** Forest plot of the pooled vascular failure rate for free fibula flap grafts. (CI: confidence interval, REML: residual maximum likelihood)  
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**Fig. 3.** Forest plot of the pooled vein thrombosis rate for free fibula flap grafts. (CI: confidence interval, REML: residual maximum likelihood)  
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(Fig. 2)

To further break down the etiologies of vascular failures, we computed pooled prevalence rates for three primary causes: venous thrombosis, arterial thrombosis, and vein compression due to hematoma. This part of the meta-analysis incorporated eight studies that cumulatively represent 1,272 grafts.

The pooled prevalence of venous thrombosis was 3% (CI 0.01-0.05). Similar to the overall failure rate, this result was subject to substantial heterogeneity ( $I^2=77.7\%$ ), reflecting considerable disparity in the rates reported across studies. (Fig. 3)

In contrast, arterial thrombosis accounted for a smaller proportion of vascular failures, with a pooled failure rate of 1% (CI 0.00-0.03). Notably, the level of heterogeneity was also lower ( $I^2=56.5\%$ ), suggestive of less variability in the rates of arterial thrombosis among the studies. (Fig. 4)

Lastly, we calculated the pooled failure rate for vein compression due to hematoma and found that it contributed to less than 1% of the overall failures, reinforcing the relatively small role of this specific complication in graft failures.

## IV. Discussion

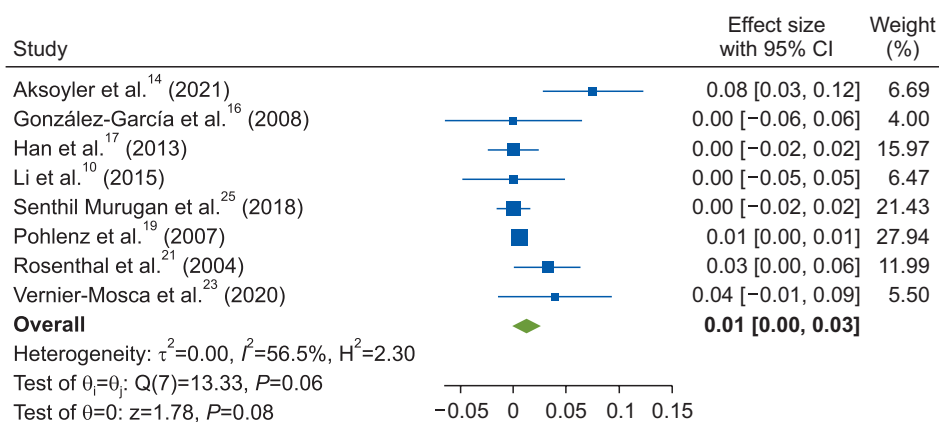
### 1. Summary of results

Our meta-analysis found an overall vascular failure rate of 6% across 11 studies involving 2,405 free fibula grafts. The substantial heterogeneity among those studies ( $I^2=93\%$ ) suggests significant variability in the reported rates of vascular failure. We also identified specific causes of vascular failure, and venous thrombosis and arterial thrombosis were the leading causes at 3% and 1%, respectively. The incidence of vein

compression due to hematoma was found to be less than 1%. Venous and arterial thrombosis pose significant challenges to the successful execution of free fibular grafts in reconstructive surgeries<sup>26</sup>. Venous thrombosis, often due to mechanical obstructions such as compression, kinking, or twisting, can lead to congestion of the graft, compromising its viability<sup>27</sup>. Rapid correction of the mechanical obstructions generally leads to high salvage rates<sup>28</sup>. However, arterial thrombosis, predominantly associated with pre-existing vascular diseases such as atherosclerosis or calcified plaques but sometimes the result of intraoperative damage or vessel size discrepancies, can lead to more severe complications. Arterial compromise is harder to identify and correct than venous issues; a swift, significant change in graft color is usually the primary indicator of a venous problem, whereas arterial problems can go unnoticed until severe ischemia occurs<sup>29</sup>.

Meta-analyses to compare different host veins and arteries, double versus single anastomoses, and the use of couplers versus hand suturing techniques were not possible.

Another issue that can introduce vascular deficiencies and lead to flap failure is blood vessel kinking, which can originate from multiple sources, such as the creation of an acute angle between the fibula axis and the pedicle, undue tension in the intraoral space, mechanical compression from hardware, inappropriate neck flexion, and erroneous pedicle positioning<sup>14,30</sup>. Each of those factors can potentially induce blood vessel kinking, thereby impairing blood flow, inducing graft congestion, and ultimately precipitating flap failure. A mitigation strategy proposed by Aksoyler et al.<sup>14</sup> involves the strategic placement of a small piece of adipose tissue around the pedicle, which serves as both a cushion to prevent vessel kinking and a guard against twisting. Our results are consistent with the literature. It has the longest vascular flap



**Fig. 4.** Forest plot of the pooled arterial thrombosis rate for free fibula flap grafts. (CI: confidence interval, REML: residual maximum likelihood)  
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Random-effects REML model

available for mandibular reconstruction. This flap is 20 to 30 cm in length, depending on the patient's size. In addition, this is a unique technique that can reconstruct bone defects from corner to corner, after several osteotomies have been performed to make the model<sup>31</sup>. Its vascular pedicle, which has a relatively stable anatomy, exhibits two vascular systems (periosteal and endosteal). This flap allows flexible molding and assembly and can be accompanied by a skin island for intraoral and extraoral reconstruction. Therefore, it supports osseointegrated implants for dental arch reconstruction and has relatively low morbidity at the donor site<sup>32</sup>. In 100% of cases in which a reconstructive plate was used, the plate was exposed to the oral cavity during the postoperative period. When small plates were used, only 4 (9.3%) of them were exposed<sup>26</sup>. The microvascular fibrous flap remains the gold standard in mandibular reconstruction because of its low loss and complication rates. The advent of small hard disks has increased the benefits of using this technique because they reduce the risk of complications<sup>26</sup>. Additionally, a case series and meta-analysis showed that the results of end to side venous anastomosis in the limbs were positive and that this technique was effective in treating differences in vein size; however, its superiority over end-to-end anastomosis could not be demonstrated<sup>27</sup>.

## 2. Factors influencing the success rate

During the surgical procedure, the anastomosis technique plays a paramount role in the success of the operation. The critical junction between the donor and recipient vessels can be achieved through couplers or hand suturing. In several studies, the coupler technique demonstrated advantages over hand suturing<sup>7</sup>. Couplers have shown a lower incidence of thrombosis, leave no foreign material in the vascular intima that could precipitate thrombosis, are less susceptible to inaccuracy and mechanical failures than hand suturing, and can overcome discrepancies up to a ratio of 3:1, thereby providing a mechanically stronger anastomosis than hand suturing<sup>10,23</sup>.

Nevertheless, it's crucial to state that couplers have not unequivocally surpassed sutures in all studies. For instance, the study by Senthil Murugan et al.<sup>25</sup> indicated a marginally higher flap success rate in the coupled anastomosis group, but the difference was not statistically significant ( $P>0.5$ ). Some retrospective studies have shown similar trends, with the success rates of coupled and sutured anastomoses being almost the same<sup>10,11</sup>. Moreover, the time-saving advantage of

couplers is questionable. In the studies of Senthil Murugan et al.<sup>25</sup> and Assoumane et al.<sup>11</sup>, the time difference of approximately 11 and 15 minutes, respectively, between sutured and coupled anastomoses was deemed clinically insignificant due to the lack of correlation between the time taken to perform anastomosis and the flap success rate.

One significant drawback of couplers is their considerable cost, which might not always be justified by the reduction in operating time<sup>10</sup>. Only in instances in which sutured anastomoses failed and re-exploration was necessary did the additional cost of the coupler balance out<sup>33</sup>. Thus, although couplers do possess certain advantages over conventional hand-sewn sutures, their effectiveness is heavily reliant on the surgeon's experience and the cost-benefit analysis for each individual patient. On the other hand, couplers are cost effective in the reconstruction of long bone defects because they achieve a higher union rate than hand-sutured fibular grafts.

The diameter of the coupler used in vein anastomosis can significantly affect the success or failure of the procedure. In the studies of Senthil Murugan et al.<sup>25</sup> and Vernier-Mosca et al.<sup>23</sup>, vein anastomosis using a coupler with a diameter of less than 2 mm introduced a high risk of venous thrombosis. For anastomosed vessels with a diameter of less than 2 mm, the recommendation is to perform the anastomosis manually, which allows the vessels to dilate. The selection of an appropriate ring size is crucial to prevent complications, such as the constriction or tearing of the vein wall or a reduction in the lumen size, which can lead to thrombosis.

Both single vein and double vein anastomosis methods have been used for free fibular grafts. Single vein anastomosis, which involves the connection of one vein from the graft to one vein at the recipient site, is often favored when there is a good match in vessel sizes and the risk of venous congestion is minimal. In contrast, double vein anastomosis, involving the connection of two veins from the graft to two veins at the recipient site, is typically used when there's a risk of venous congestion due to size mismatch or when the venous outflow is anticipated to be high<sup>17,34</sup>. The intent behind double vein anastomosis is to escalate outflow capacity and mitigate the risk of venous thrombosis. Nevertheless, the studies of Assoumane et al.<sup>11</sup> and Han et al.<sup>17</sup> revealed no significant difference in the vascular failure rate between free fibular grafts anastomosed using the double vein and single-vein methods. Although flap failure was comparable between flap anastomoses performed using a venous coupler and those performed using a conventional suture technique, findings revealed that the total number of venous thrombosis cases was

higher in the coupler-anastomosis group. Therefore, microsurgeons should remember that these devices involve specific techniques and challenges not normally seen in hand joining. Especially at the early stages of the learning process, their application must be questioned critically and limited to clearly defined situations<sup>35</sup>. Using couplers for venous anastomosis in head and neck free flap reconstruction influences surgical planning and procedures. Research results show that using a vein graft device in head and neck free flap reconstruction does not change the rate of flap necrosis. However, the use of an implant device can reduce overall procedure time<sup>36</sup>.

The task of reconstructive surgery, especially in the maxillofacial region, can be significantly complicated by the limited availability of recipient blood vessels due to factors such as tumor invasion and previous surgeries. The choice of veins and arteries for anastomosis is influenced by factors such as the size of the graft blood vessel, its proximity to the excision area, and the quality of the graft vessels<sup>37,38</sup>. In the studies we reviewed, the most commonly used graft artery for free fibular grafts was the peroneal artery, and the most common recipient arteries were the superior thyroid artery and the facial artery. In terms of veins, the peroneal vein in the graft and branches of the internal and external jugular veins in the recipient site were the most commonly used.

Despite the methodical selection of recipient vessels, several challenges persist. In particular, previously dissected and irradiated zones can restrict anastomosis possibilities. Prior exposure to radiation therapy and cervical dissections can lead to radicular fibrosis and scar tissue, which can significantly limit the options for successful anastomosis and contribute to a host of complications<sup>39</sup>. In the study conducted by Li et al.<sup>10</sup>, two out of three reported cases of vein thrombosis occurred in patients who had undergone radiotherapy prior to the anastomosis procedure.

The success of an anastomosis procedure can be significantly affected by the quality of the recipient vessels. One major cause of failure, venous thrombosis, is often linked to issues such as poor quality of recipient vessels due to prior irradiation, the thinness of the recipient vessels, and a mismatch in the diameter of the vessels<sup>39</sup>. The latter necessitates a high level of skill and time to prevent fluctuations in blood flow and intraluminal protrusions of the wall, which can cause thrombosis, and ensure successful anastomosis. The use of microvascular coupling can be a viable strategy to compensate for this discrepancy, prevent vasospasm, and reduce anastomosis time.

In addition to those complications, some patients pres-

ent with systemic blood clotting disorders, such as thrombophilia, which can dramatically increase the risk of vein thrombosis post-anastomosis<sup>40</sup>. Hereditary (e.g., Factor V Leiden mutation, prothrombin gene mutation) or acquired (e.g., antiphospholipid syndrome) thrombophilic conditions can predispose patients to hypercoagulability, leading to a high risk of clot formation that can occlude the anastomosis site. Similarly, conditions such as von Willebrand disease can affect clotting by causing deficiencies in clotting factors that make it challenging to achieve hemostasis after surgery and can lead to anastomotic leakage<sup>41</sup>. Therefore, a comprehensive preoperative evaluation, including a thorough review of the patient's medical history, previous treatments, and possible coagulation disorders, is vital to the success and durability of an anastomosis procedure.

### 3. Pre- and postoperative evaluations of the anastomosis procedure

In the postoperative phase, the monitoring and care of anastomoses is vitally important. In the studies we reviewed, multiple methodologies were used to ensure the success and viability of the procedure, including monitoring blood flow changes based on transit-time flow measurements and the use of color Doppler ultrasound<sup>20,42</sup>. However, flap perfusion rates can vary due to factors such as the type of flap, the donor and recipient sites, the patient's general health condition, vascular diseases, nicotine abuse, and previous surgeries. Therefore, it's recommended that preoperative examinations be conducted, including computed tomography or magnetic resonance angiography of the head, neck, and donor site, to ensure a comprehensive understanding of the vascular situation<sup>43,44</sup>.

Postoperatively, the heart rate and mean arterial blood pressure should be closely monitored, but it is worth noting that these measurements do not always correlate with the flap's arterial perfusion. Furthermore, the effects of variations in arterial perfusion caused by factors such as nicotine consumption, type II diabetes, and transplant loss need to be acknowledged<sup>45</sup>.

Given the dynamic nature of the circulatory system, each anastomosis case presents unique challenges. The patient should keep their head elevated on two pillows whenever they lie down for two weeks to help reduce swelling. The patient can also gently apply an ice pack to the wound for 10 minutes, three or four times an hour for the first 24 hours. This will help reduce swelling, but it is not effective after 24

hours. The frequency of clinical monitoring during the early postoperative period varies between centers, but clinical flap checks are typically performed every 2 to 4 hours during the first 2 to 3 days after surgery. To date, the gold standard for FFF monitoring includes clinical examination (i.e., flap color, capillary refill, tissue tension, temperature) and handheld acoustic Doppler ultrasound. Postoperative care and monitoring should reflect a detailed understanding of flap physiology, individual patient factors, and previously determined reference values. By adopting this meticulous and comprehensive approach, a stable vascular supply, successful healing, and optimal patient outcomes following anastomosis can be ensured.

In summary, clinical follow-up remains the gold standard for postoperative free flap evaluation. Other adjuvants might be useful to surgeons and medical teams, but there is no clear consensus regarding their appropriate use. Like many postoperative treatment regimens, free flap follow-up technique is surgeon-dependent and can vary significantly between institutions.

#### 4. Limitations and suggestions for further research

This review has several limitations. The meta-analyses in our review displayed a significant level of heterogeneity, indicating considerable variation in vascular failure rates among the studies. Therefore, the pooled estimates might not accurately represent the true prevalence due to differences among the individual studies in sample size, study methodology, or other factors. Evaluating and addressing bias is crucial for ensuring research credibility and generalizability. Although it was unfortunate to find a range of bias across the studies we found in the literature, it is a valuable discovery in itself that highlights the need for further investigation and improvements in the methodologies used in future studies. Also, due to insufficient data, we were unable to compare the effects of different host veins and arteries, double versus single anastomoses, and the use of couplers versus hand suturing techniques.

Moreover, the results might be subject to various forms of bias, particularly in the retrospective studies, where a lack of randomization and blinding could also bias the results. We did not consider patient-level factors, such as underlying health conditions, previous surgeries, the extent of tissue damage, and patient lifestyle, which can all affect the success rate of anastomosis. Our focus solely on free fibula grafts might also limit the generalizability of the results to other

types of grafts or reconstructive surgeries. Our inclusion criteria targeted retrospective or prospective cohort studies and clinical studies investigating dental and functional rehabilitation outcomes in human subjects undergoing maxillofacial reconstruction using microvascular flaps. We excluded case-control studies, studies of alternative reconstruction methods, and animal investigations.

Given those limitations, future research should include more comprehensive comparative studies that assess different techniques, host veins, arteries, and grafts. Economic evaluations considering the significant cost difference between couplers and hand suturing techniques would also be beneficial. Additionally, future studies should incorporate individual patient factors, including coagulation disorders, previous radiotherapy, the extent of tissue damage, and lifestyle factors that could potentially affect the outcomes. Further long-term follow-up research of patients undergoing anastomosis could provide valuable insights into the durability of different techniques and the prevalence of late complications. By addressing these limitations and incorporating these suggestions, future research can contribute significantly to improving the success rates of anastomosis in reconstructive surgery.

## V. Conclusion

This systematic review and meta-analysis presents an in-depth evaluation of vascular failure rates in microvascular reconstruction surgeries involving free fibula grafts. We found a 6% overall vascular failure rate across the reviewed studies, with substantial heterogeneity suggesting significant variability in the reported rates of vascular failure. The findings indicate that vein thrombosis (3%) and arterial thrombosis (1%) were the leading specific causes of vascular failure. Our analysis highlights the complex interplay of multiple factors such as the technique of anastomosis, the quality of recipient vessels, the use of couplers versus hand suturing, and the diameter of the coupler in influencing the success of anastomosis.

Despite the potential advantages of couplers in most situations, our study suggests that their superiority over sutures is not consistently demonstrated across all studies, underlining the importance of considering individual patient characteristics and procedural specifics. Similarly, although both single and double vein anastomoses have merits and drawbacks, their efficacy seemed to be similar in terms of vascular failure rates in free fibular grafts.

Our study also underscores the importance of compre-

hensive preoperative evaluation, meticulous operative techniques, and thorough postoperative care and monitoring for optimal patient outcomes following anastomosis.

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## Authors' Contributions

H.M. and S.S. participated in data collection and wrote the manuscript. M.H.K.M. and R.T. participated in the study design and performed the statistical analysis. E.T. and S.H. participated in the study design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

## Funding

No funding to declare.

## Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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**How to cite this article:** Tahmasebi E, Hajisadeghi S, Shafiei S, Moslemi H, Kalantar Motamedi MH, Tabrizi R. Factors affecting anastomosis failure in microvascular fibula flap reconstruction of the maxillofacial region: a systematic review and meta-analysis. *J Korean Assoc Oral Maxillofac Surg* 2025;51:3-16. <https://doi.org/10.5125/jkaoms.2025.51.1.3>