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Review

The use of vascularized fibula flap in mandibular reconstruction; A comprehensive systematic review and meta-analysis of the observational studies

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ABSTRACT

Background: Vascularized fibular flaps are considered the gold standard for the reconstruction of segmental defects in the mandible. This review compares the complication and success rates of these techniques between primary and secondary reconstruction, as well as between lateral and antero-lateral defects.

Type of studies reviewed: A systematic review and meta-analysis were conducted according to PRISMA protocol and the Cochrane Handbook for Systematic Reviews of Interventions. The authors performed an independent comprehensive search using PubMed, Ovid MEDLINE, Web of Science, the Cochrane Central Register of Controlled Trials, ClinicalTrials.gov and COS Conference Papers Index according to established inclusion and exclusion criteria. The methodological index for nonrandomized studies (MINORS) was used to assess the quality of the included studies. Meta-analysis was conducted to compare the type of reconstruction and location of the defect.

Results: Seventy-eight studies, involving 2461 patients, were eligible. 83.7% of the included patient received primary reconstruction with vascularized fibular flap. The overall flap success rate was 93%. There was improvement in MINORS quality score over time with positive correlation with the publication year ($r = 0.5549$, $P < 0.0001$, CI 0.3693 to 0.6979). Meta-analysis indicated no significant association in flap success between primary and secondary reconstruction, or lateral and antero-lateral defects.

Conclusion: Based on the available studies, this review found no evidence of difference in success or complication rates between primary and secondary reconstruction or between lateral and anterolateral defects. High-quality clinical studies are required to analyze the outcome of these techniques, especially regarding the impact of chemotherapy, radiation therapy, implant-supported dental prostheses, and preoperative planning, on the outcome of reconstruction.

1. Introduction

Integrity of the mandibular arch is a major determinant of facial esthetics. An intact mandible is also important for various functions, such as verbalization, mastication, deglutination, and airway support. These functions can be compromised due to loss or removal of a segment of the mandibular bone, for example after surgical resection of an oral cavity tumors, osteomyelitis, massive trauma, or osteoradionecrosis, resulting in a segmental defect (Thorne and Smith, 2007).

The reconstruction of bony continuity of the mandible, as well as its soft tissue coverage, can be achieved using non-vascularized grafts or free vascularized bone flaps. Autogenous sources for the

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grafts have included ribs (Serafin et al., 1977), fibula (Hidalgo and Rekow, 1995), radius (Vaughan, 1994), iliac crest (David et al., 1988), and scapula (Sullivan et al., 1989; Foster et al., 1999). Vascularized bone flaps have been the gold standard for large segmental bone defects (Fernandes, 2006; Takushima et al., 2001). The percentages of bony union in vascularized bone flaps (VBF) and non-vascularized bone grafts (NVBG) have been 96% and 69% respectively (Foster et al., 1999; Pogrel et al., 1997). In addition, VBF showed better aesthetic and functional scores as compared to NVBG (King et al., 2002).

Taylor and colleagues introduced vascularized free fibular flap as an available source of bony reconstruction for the first time in 1975 (Taylor et al., 1975). Chen and his colleagues described the harvesting the osteo-cutaneous fibula flap in 1983 (Chen and Yan, 1983). In 1989, Hidalgo and colleagues presented the results of mandibular reconstruction in 13 patients using vascularized fibula flap (Hidalgo, 1989). Since that time, the use of vascularized fibula flap has become the technique of choice for structural and functional reconstruction of the mandible with large segmental defects (Sieg et al., 2002). Osteo-cutaneous fibular free flaps provide viable bone with its soft tissue coverage for up to 20 cm (Hidalgo, 1989; Wei et al., 1994).

However, VBG have been associated with many latent risks and potential complications, as the viability of the graft is mainly dependent on a delicate microsurgical technique for the arterial and venous anastomoses. Furthermore, around 20% of VBG are associated with incidence of fracture as a late postoperative complication (de Boer and Wood, 1989; Minami et al., 1993). In addition, several trials have reported donor-related complications if the harvest technique was not performed appropriately such as leg instability, peripheral vascular disease, or valgus deformity (Kanaya et al., 2002; Shpitzer et al., 1997). Some studies demonstrated that when the reconstructions are performed immediately (primary reconstruction), patients experienced better long term functional and aesthetic outcomes, compared to those who had delayed (secondary) reconstruction (Schusterman et al., 1993; Markowitz et al., 1994). In 1992, a study reported that primary reconstruction was associated with shorter hospital stays, lower costs and 50% less complication rate than secondary reconstruction (Kroll et al., 1992). Although primary and secondary reconstruction using VBF had been performed to thousands of patients over the past decades, only few studies analyzed the difference between both of them in term of patients' outcomes.

The current systematic review and meta-analysis aimed to evaluate the outcome of mandibular reconstruction after segmental mandibular defects in patients who experienced either tumor resection, trauma, osteomyelitis, or osteoradionecrosis. Meta-analysis compared primary outcome [flap success] between primary and secondary reconstruction cases and secondary outcomes [flap-related complications incidence] between two different mandibular reconstruction sites: lateral (linear) and Anterolateral (curved) defects.

2. Methods

2.1. Protocol

The study protocol was designed according to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) Statement and follow the guidelines of Cochrane Handbook for Systematic Reviews of Interventions (Higgins, 2011).

2.2. Search strategy

Two authors (MA and PS) independently conducted a search of the electronic databases at two different time point in PubMed, Ovid MEDLINE, Web of Science, the Cochrane Central Register of Controlled Trials, ClinicalTrials.gov and COS Conference Papers Index. PubMed was searched for in-process and non-indexed records. The Boolean operations and keywords used for the search; ((("mandible" [MeSH Major Topic] OR ("mandibular reconstruction" [MeSH Terms] OR ("mandibular" [All Fields] AND "reconstruction" [All Fields]) OR "mandibular reconstruction" [All Fields])) AND "fibula" [MeSH Major Topic]) OR (Vascularized [All Fields] AND ("transplants" [MeSH Terms] OR "transplants" [All Fields] OR "graft" [All Fields]))) AND ("free tissue flaps" [MeSH Terms] OR ("free" [All Fields] AND "tissue" [All Fields] AND "flaps" [All Fields]) OR "free tissue flaps" [All Fields] OR ("free" [All Fields] AND "flap" [All Fields]) OR "free flap" [All Fields]). The search strategy was a combination of subject headings and free text words in Ovid MEDLINE, topic searching in Web of Science, and free text words in the remaining databases (see Fig. 1). Records were de-duplicated. Study reviewers performed manual searching on available bibliographies of retrieved documents.

2.3. Study selection and eligibility criteria

Two independent reviewers examined and analyzed article titles, article abstracts, and full-text documents for eligibility criteria:

2.3.1. Inclusion criteria

1. **Type of studies:** Randomized controlled trials, cohort studies, non-randomized clinical trials, cases series and case reports including more than five patients. The intervention involved mandibular reconstruction with vascularized fibula flap.

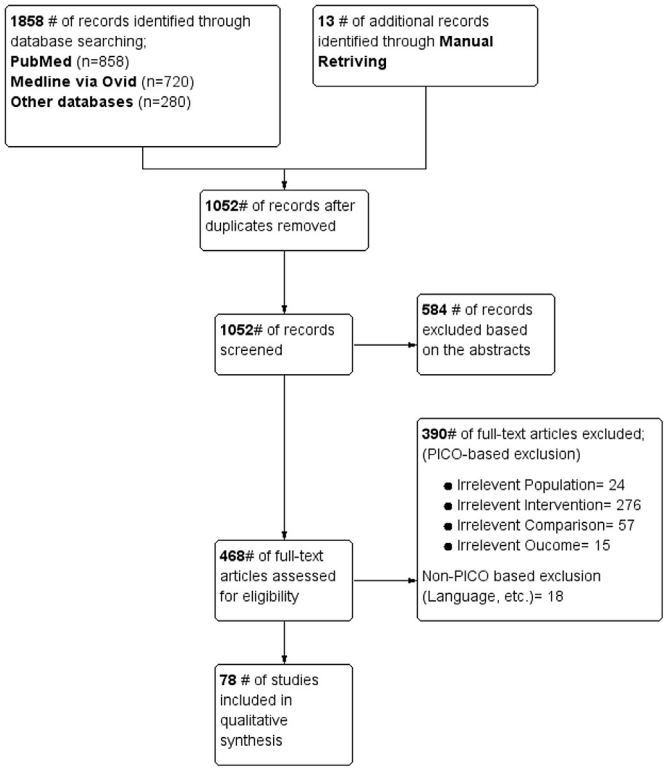

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart.

2. **Type of Participants:** An eligible study should have at least five subjects who had a segmental mandibular defect after tumor resection, trauma, osteomyelitis, or osteoradionecrosis. Segmental defects are defined as full-thickness defects where the remaining mandibular stumps lose any continuity with each other.
3. **Type of interventions:** Studies must include reconstruction of segmental mandibular defects using vascularized fibular grafts, either alone or compared to another reconstruction method. Reconstruction was considered primary when the bone transfer occurred at the same setting as defect creation or at the initial surgical procedure immediately following trauma. It was considered secondary when bone transfer was delayed to a separate session, regardless of the length of delay. Lateral defects were defined as not involving the anterior curvature of the para-symphyseal and symphyseal regions, while antero-lateral defects included these curvilinear regions.
4. **Type of comparison and Outcome measures:** Studies must include a follow-up period of at least six months following surgery. Outcome analysis must evaluate the flap suvival (success; primary outcome) between primary and secondary reconstruction settings and/or flap-related complications (secondary outcome) between lateral and antero-lateral defects.

2.3.2. Exclusion criteria

Non-human studies, narrative reviews, non-segmental defects, and surgical intervention not including vascularized fibula flap.

Study inclusion required both reviewers to agree (MA and AA). Disagreements were resolved by direct communication between the two reviewers.

2.4. Data collection and data items

Data were extracted independently by two reviewers (MA, and AA). A standard form was used; the extracted items included the following: (1) Patients characteristics and demographics, (2) type of reconstruction (primary or secondary), (3) flap characteristics (free or double), (4) mandibular defect size, (5) cause of defect, (6) flap survival rate, and (7) complications of the surgery, (8) Radiochemotherapy characteristics, (9) mandibular defect site, (10) Fixation plate, (11) Use of Dental implants, (12) Patients survival and (13) Post-reconstruction aesthetic function and dietary function (Tables 2–5).

Table 1
Total methodological index for non-randomized studies (MINORS) score.

Methodological Items for non-randomized studies	Average	SD	Range
(1) A clearly stated aim	1.551282	0.616809	0–2
(2) Inclusion of consecutive patients	1.384615	0.607972	0–2
(3) Prospective collection of data	0.166667	0.37509	0–1
(4) Endpoints appropriate to the aim of the study	1.397436	0.610296	0–2
(5) Unbiased assessment of the study end point	0.858974	0.502574	0–2
(6) Follow up period appropriate to the aim of the study	1.628205	0.666625	0–2
(7) Loss to follow-up less than 5%	1.410256	0.653381	0–2
(8) Prospective calculation of the study size	0.012821	0.113228	0–1
Total for non-comparative (16)	8.410256	2.2182	4–12
Additional criteria in the case of comparative study			
(9) An adequate control group	0.25641	0.612338	0–2
(10) Contemporary groups	0.217949	0.473929	0–2
(11) Baseline equivalence of groups	0.153846	0.397294	0–2
(12) Adequate statistical analyses	0.102564	0.381036	0–2
Total score (24)	9.141026	2.680978	4–18

2.5. Quality assessment of included studies

The methodological index for nonrandomized studies (MINORS) was used to assess the quality of the included studies (Slim et al., 2003). Twelve items were scored as “0” (not reported), “1” (reported but inadequate), or “2” (reported and adequate). Two reviewers independently assessed the quality of the included studies (Table 1).

2.6. Statistical analysis

Standard meta-analytic methods were used to combine the results of all studies that provided sufficient data in order to obtain overall effect size estimates and the corresponding forest plots. For studies in which either all of the subjects or none of the subjects experienced the outcome of interest in either of the groups, Agresti's method (Agresti, 2007, p. 16) was used to estimate the odds ratio and obtain a 95% confidence interval prior to performing the meta-analysis. Cochran's Q statistic was used to assess heterogeneity of the studies, and publication bias was assessed using funnel plots and fail-save analyses. All calculations were carried out using Comprehensive Meta-Analysis 2.2.064 (www.Meta-Analysis.com, 2011) (Comprehensive Meta-analysis software (CMA)).

3. Results

3.1. Study selection

Based on our search strategy, 1858 publications were identified. In addition, 13 records were identified through manual references retrieving. After removal of duplicates, 1052 records were screened based on the inclusion criteria. After initial screening, 584 studies were excluded based on the abstract and 390 studies were excluded after applying the exclusion criteria on the full-text studies. The study selection process ended up with 78 included studies (Fig. 1).

3.2. Participants characteristics

The selected 78 studies included 2461 patients. The mean age across trials which addressed their patients' age was 48.18 years old ranged from 7.8 to 60.9 years. About 67.9% of the included patients were male. The most common cause of segmental defect was surgical resection of squamous cell carcinoma (1745 patients). Out of 638 patients who received perioperative radiotherapy, chemotherapy, or both, 525 received radiotherapy alone.

3.3. Intervention characteristics

Primary reconstruction was performed in 83.7% of patients, while 243 patients had a secondary reconstruction. Reconstruction was done either by straight free flap or double-barrel flap in 88.3% and 11.7% respectively. Lateral mandibular defect “L” was reported in 45% of patients. Other sites included: central “C”, lateral-central ”LC”, lateral-center-lateral “LCL”, hemi-mandibular “H”, or even called “HC and HCL” when the defect extends beyond the midline to involve either the whole symphysis and/or a part of the other mandible body). Out of the included studies, 65 reported internal fixation using metal plates. Titanium reconstruction plate were used in 41 studies involving 1072 patients. Twenty studies-including 670 patients-reported the use of mini-plate as proper fixation method. Out of 446 patients who received postoperative either radiotherapy or chemotherapy or both, 398 received radiotherapy alone.

Table 2
Sub group stratification of postoperative characteristics in the studies that didn't use versus used radio-chemotherapy perioperatively.

Author	Patients No.	Flap success %	Complications									MINORS
			Fistula	Necrosis	Flap loss	Donor- site	Plate	Infection	Wound dehiscence	Others	% of Complications	(Score)
Studies that did not use radio- and chemotherapy peri-operatively												
Ang	13	95%	1	1	0	0	0	0	0	0	15%	9
Bahr	8	100%	NA	NA	NA	NA	NA	NA	NA	NA	0%	5
Bianchi	17	76%	3	1	0	0	0	0	0	0	24%	11
Bianchi	17	100%	NA	NA	NA	NA	NA	NA	NA	NA	0%	12
Chen	14	92.80%	0	0	2	0	0	0	1	3	43%	5
Chang	12	100%	NA	NA	NA	NA	NA	NA	NA	NA	0%	4
Chang	114	98.30%	NA	NA	NA	NA	NA	NA	NA	NA	0%	10
Coredio	150	100%	NA	NA	NA	NA	NA	NA	NA	NA	0%	7
Caballero	7	100%	0	0	0	0	0	0	0	2	29%	8
Dean Ad	11	45.50%	0	0	0	0	1	0	0	0	9%	6
Demirkan	7	NA	0	1	0	0	0	2	0	0	43%	4
Fan	30	100%	5	1	0	0	0	0	0	0	20%	11
Ferrari	14	NA	0	1	0	2	0	5	0	1	64%	12
Ferri	29	86.20%	NA	NA	NA	NA	NA	NA	NA	NA	0%	6
Fujiki	38	94.70%	4	0	2	17	0	5	2	0	79%	15
Gabr	17	82.30%	1	0	2	0	0	5	0	2	59%	7
Gabr	17	100%	0	0	0	0	0	0	0	13	76%	11
Gonzales	42	83.32%	0	0	0	0	0	0	0	5	12%	11
Hakim	37	91.60%	NA	NA	NA	NA	NA	NA	NA	NA	0%	12
Head	210	93.30%	NA	NA	NA	NA	NA	NA	NA	NA	0%	9
Hidalgo	60	NA	4	0	0	10	2	0	0	0	27%	7
Irjala	10	90%	0	0	1	0	0	0	0	0	10%	9
Kannan	10	100%	0	2	0	0	0	0	1	2	50%	9
Kim	7	NA	NA	NA	NA	NA	NA	NA	NA	NA	0%	11
Li	6	100%	NA	NA	NA	NA	**NA**	NA	NA	NA	0%	11
Miyamoto	10	100%	1	0	0	3	0	3	0	1	80%	18
Nakayama	8	84.60%	0	1	0	0	0	2	0	0	38%	5
Nikolaos	23	100%	0	0	0	12	0	0	0	0	52%	7
Ooi	30	97%	0	0	0	0	0	5	0	2	23%	10
Pelad	13	85%	0	0	2	4	0	0	0	0	46%	11
Philipis	**11**	NA	NA	NA	NA	NA	NA	NA	NA	NA	0%	10
Politi	11	90.90%	0	0	0	0	0	0	0	1	9%	14
Pogrel	38	94.90%	0	0	2	0	0	0	0	0	5%	10
Sakuraba	101	94%	0	29	0	0	0	0	0	0	29%	9
Santamaria	12	100%	1	1	2	0	0	0	0	0	33%	5
Shpitzer	47	91.50%	0	0	0	1	4	0	0	0	11%	10
Suh	40	100%	6	0	0	2	17	7	0	22	135%	9
Shen ‘15	10	NA	NA	NA	NA	NA	NA	NA	NA	NA	0%	10
Shen ‘13	45	97.78%	0	0	3	0	6	0	0	0	20%	6
Shen	10	NA	NA	NA	NA	NA	NA	NA	NA	NA	0%	9
Store	7	71.40%	NA	NA	NA	NA	NA	NA	NA	NA	0%	9
Trignano	34	76.47%	6	8	0	0	0	5	10	1	88%	10
Tsuchiya	52	88.59%	0	2	0	0	8	2	0	0	23%	11
Van Germet	46	100%	4	2	0	0	4	0	0	0	22%	14
Vayvada	11	100%	0	0	0	0	0	0	0	2	18%	10
Wang	10	100%	0	0	0	0	0	1	0	0	10%	10
Wei 1998	36	93%	0	0	0	5	0	1	5	0	31%	6
Yilmaz	13	100%	0	0	0	1	0	0	0	3	31%	9
Studies that used radio- and chemotherapy peri-operatively												
Antony	17	82%	0	0	0	3	0	0	0	5	47%	6
Avraham	52	92.60%	0	0	4	0	0	0	0	14	35%	6
Baron	5	100%	0	1	0	0	0	0	0	1	40%	9
Boyed	31	NA	NA	NA	NA	NA	NA	NA	NA	NA	0%	10
Chaine	9	88.80%	5	3	2	0	0	0	5	0	167%	11
Chao	6	100%	0	0	0	0	0	0	0	1	17%	11
Cheng	17	100%	0	2	0	0	0	0	1	0	18%	8
Cheung	12	100%	0	0	0	2	0	0	0	0	17%	5
Crosby	11	81.80%	0	0	1	4	0	2	0	5	109%	11
Disa	35	97%	NA	NA	NA	NA	____	NA	NA	NA	0%	7
Farwell	184	79.90%	0	0	0	0	37	16	0	0	29%	9
Haughey	9	88.80%	0	1	1	0	0	0	0	0	22%	11
He	7	100%	NA	NA	NA	NA	NA	NA	NA	NA	0%	9
Heller	5	91.30%	NA	NA	NA	NA	NA	NA	NA	NA	0%	7
Hidalgo	12	100%	0	1	0	2	0	0	0	0	25%	7
Inbal	5	100%	0	0	1	4	0	0	0	0	100%	10
Jeng	10	100%	0	0	0	0	0	3	0	1	40%	9
Jeng	8	96%	0	1	0	0	0	1	0	0	25%	11
Knott	101	85.10%	NA	NA	NA	NA	NA	NA	NA	NA	0%	8
Lee	22	100%	1	0	0	0	0	1	1	0	14%	8
Lee	14	92.80%	0	0	0	6	0	0	0	0	43%	6
Posch	12	96%	0	0	0	0	2	0	0	3	42%	9
Serra	6	NA	NA	NA	NA	NA	NA	NA	NA	NA	0%	6

Table 2 (*continued*)

Author	Patients No.	Flap success %	Complications									MINORS
			Fistula	Necrosis	Flap loss	Donor- site	Plate	Infection	Wound dehiscence	Others	% of Complications	(Score)
Shan	5	90%	NA	NA	NA	NA	NA	NA	NA	NA	0%	11
Shpitzer	57	84.20%	0	1	0	13	7	3	5	3	56%	10
Virigin	168	96.60%	0	0	4	5	0	0	0	7	10%	13
Wei 2003	20	90%	1	0	2	0	0	0	0	0	15%	9
Wei	27	96.30%	0	0	1	0	0	2	4	1	30%	7
Wolff	24	95.80%	NA	NA	NA	NA	NA	NA	NA	NA	0%	7
Zender	54	90%	0	9	0	0	0	10	0	13	59%	9

Table 3
Post-reconstruction Aesthetic–Function and dietary habits with or without dental implants.

Author	Patients No.	Dental Implants	Post-reconstruction Aesthetic–Function						Excellent %
			Excellent	Good	Acceptable	Unacceptable	Not evaluated	Evaluated/Total	
[1] With Dental Implants									
Antony	17	6	9	5	2	1	0	17\17	53%
Bianchi	17	17	2	0	6	0	9	8\17	12%
Cheung	12	1	3	7	1	1	0	12\12	25%
Coredio	150	20	42	36	36	19	17	133\150	28%
Ferrari	14	14	0	10	2	2	0	14\14	0%
Gonzales	42	11	0	38	0	3	1	42\42	0%
Hidalgo	60	34	0	29	18	13	0	60\60	0%
Li	6	6	4	2	0	0	0	6\6	67%
Ooi	30	3	14	0	11	1	4	26\30	47%
Politi	11	10	10	0	1	0	0	24\24	91%
Vayvada	11	3	11	0	0	0	0	11\11	100%
Yilmaz	13	4	9		2	0	2	11\13	69%
[2] Without Dental implant									
Cheng	17	NA	6	3	1	2	5	12\17	35%
Dean Ad	11	NA	0	10	0	1	0	11\11	0%
Ferri	29	NA	0	25	0	4	0	29\29	0%
Gabr	9	NA	2	5	2	0	0	9\9	22%
Sakuraba	101	NA	42	0	0	0	59	42\101	42%
Shpitzer	47	NA	28	0	18	2	0	47\47	60%
Author	Patients No.	Dental Implants	Post-reconstruction Dietary habit						Regular %
			Regular	Soft	Liquid	GA tube	Not mentioned	Total evaluated	
[1] With Dental Implants									
Antony	17	6	11	5	0	1	0	17\17	65%
Boyed	31	2	11	15	3	2	0	31\31	35%
Coredio	150	20	60	60	7	6	17	133\150	40%
Crosby	11	11	11	0	0	0	0	11\11	100%
Ferrari	14	14	12	1	0	1	0	14\14	86%
Hidalgo	60	34	0	5	4	0	8	9\17	0%
Li	6	6	6	0	0	0	0	6\6	100%
Ooi	30	3	23	2	1	0	4	26\30	77%
Politi	12	10	7	4	1	0	0	12\12	58%
Vayvada	11	3	11	0	0	0	0	11\11	100%
Virigin	168	38	23	37	0	32	76	92\168	14%
[2] Without Dental implant									
Baron	5	NA	4	0	0	0	1	4\5	80%
Gabr	60	NA	23	19	0	3	0	45\60	38%
Miyamoto	10	NA	0	8	1	2	0	11\11	0%
Sakuraba	101	NA	37	7	0	0	57	44\101	37%
Shpitzer	47	NA	30	13	0	5	0	48\48	64%

3.4. Outcome assessment characteristics

A total of 2305 patients were reconstructed with vascularized fibular flap with 93% success rate with a range of 45.5%–100%. The mean duration of follow-up (reported in 58 studies, involving 1976 patients) was 40 months, with a range of 1.5–144 month. At the end of the follow up period, 1112 out of 1293 patients survived (survival data was included only in 46 studies).

Data about post-reconstruction complications was reported in 56 studies, involving 1619 patients. Flap-related complications included fistula formation, necrosis, flap loss, and plate exposure in 43, 69, 32 and 88 patients respectively. In addition, 81 patients had wound infection post-operatively, with overt wound dehiscence reported in 35 patients. Donor-site morbidity was reported in 96 patients, such as ankle instability, paresthesia, partial skin graft loss, wound infection and dehiscence, and seroma. Serious systemic complications were reported in 114 patients, including deep venous thrombosis, pneumonia, and cardiovascular complications postoperatively as a result of calf muscle morbidity.

Only 34 studies reported dental rehabilitation following reconstruction. A total of 1033patients received dental

Table 4
Details about the patient and flap characteristics.

Study	Mean Age	Type of Reconstruction		Defect size	Flap characteristics		Dental Implants	Flap Success rate	Patient Survival	Follow up
	(Years)	Primary	Secondary	(CM)	Single flap	Double flap	Ptn. received			(months)
Ang	46.7	7	6	NM	13	0	1	95%	86%	26.9
Antony	54	NM	NM	6.3	17	0	6	82%	94%	NM
Avraham	44.2	NM	NM	NA	36	16	30	92.60%	100%	33.6
Bahr	42	8	0	4.8–11	0	8	NM	100%	100%	NM
Baron	55.8	NM	NM	NM	5	0	NM	100%	NM	NM
Bianchi	50.9	NM	NM	5.6	6	11	NM	76%	47%	53.6
Bianchi	52.3	13	4	NM	17	0	17	100%	100%	63
Boyed	57.8	NM	NM	9	31	0	2	NM	NM	11.7
Chaine	35	9	0	9.8	9	0	2	88.80%	100.00%	53
Chen	54.3	14	0	16.2	14	0	NM	92.80%	64.20%	25.7
Chang	36.3	12	0	8.1	12	0	12	100%	NM	25
Chang	49.5	92	24	8.9	114	0	NM	98.30%	NM	25
Chao	48.3	NM	NM	9.2	6	0	NM	100%	100%	10.8
Cheng	50.5	NM	NM	NM	17	0	NM	100%	NA	25.3
Cheung	57	11	1	14.5	12	0	1	100%	92%	10
Coredio	50	146	4	NM	135	0	20	100%	NM	120
Crosby	14	6	5	9	11	0	11	81.80%	90.90%	41
Caballero	9.1	6	1	NA	7	0	NM	100%	100%	18–60
Dean Ad	55	11	0	7.68	11	0	NM	45.50%	NM	NM
Demirkan	54	7	0	NM	7	0	NM	NM	57.10%	NM
Disa	42	35	0	———	35	0	17	97%	NM	47
Fan	46.8	0	31	NM	31	0	NM	100%	100%	NM
Farwell	60.9	180	4	NA	145	0	NM	79.90%	NM	NM
Ferrari	50	7	7	NA	14	0	NM	NM	NM	110.4
Ferri	50.6	23	6	11.5	29	0	NM	86.20%	100%	NA
Fujiki	57	NM	NM	NA	38	0	NM	94.70%	NM	84
Gabr	57.66	17	0	8.13	17	0	NM	82.30%	NM	NM
Gabr	55.12	17	0	8.79	17	0	NM	100%	94.10%	NM
Gonzales	54.39	35	7	NM	38	0	11	83.32%	92.85%	60
Hakim	51.8	23	14	NA	37	0	29	91.60%	NM	94.5
Haughey	64.3	NM	NM	NA	9	0	6	88.80%	NM	NM
He	51.5	6	1	8	7	0	NA	100%	88.20%	25
Head	NM	NM	NM	NM	NM	NM	NM	93.30%	98.10%	21.5
Heller	67	5	0	NA	5	0	NM	91.30%	74%	NM
Hidalgo	NM	NM	NM	13.6	NM	NM	NM	100%	NM	NM
Hidalgo	46.7	NA	NA	9.4	NA	0	34	NM	98%	39.2
Irjala	60	NM	NM	NM	9	0	4	90%	60%	51.5
Inbal	50.8	5	0	NM	5	0	NM	100%	60%	NM
Jeng	51.7	10	0	9.4	0	10	NM	100%	90%	24
Jeng	53.5	8	0	9.12	8	0	NM	96%	81%	12
Knott	NM	70	31	8.1	NA	NA	NM	85.10%	NM	14.6
Kannan	63	NM	NM	7	10	0	1	100%	91.60%	NM
Kim	48	0	7	7	7	0	NM	NM	NM	60
Li	13.3	6	0	10	6	0	6	100%	100%	24.2
Lee	37	13	9	8	22	0	5	100%	100%	16.4
Lee	48	7	7	16.7	14	0	3	92.80%	80%	19.9
Miyamoto	52.6	7	3	NM	0	10	NM	100%	21.73%	30.5
Nakayama	64	4	4	NM	8	0	NM	84.60%	100%	NM
Nikolaos	52.7	12	11	15.1	7	16	9	100%	100%	15.6
Ooi	27.3	29	1	8.2	30	0	3	97%	NA	59
Pelad	49.3	6	7	9.3	13	0	2	85%	100%	27.9
Philipis	7.8	11	0	NM	11	0	NM	NA	90.90%	24–144
Posch	63	5	7	10	0	12	NM	96%	100%	24
Politi	56	11	0	9.5	11	0	10	90.90%	NM	12
Pogrel	46.9	36	2	9.1	38	0	8	94.90%	100%	24
Sakuraba	57.2	NA	NA	NM	79	22	NM	94%	61%	33.6
Santamaria	46.25	NM	NM	8	12	0	NM	100%	NA	46.8
Serra	41.6	NM	NM	NM	NA	NA	NM	NA	NA	13.6
Shan	50.4	0	5	NM	5	0	NM	90%	100%	49
Shpitzer	55.6	NM	NM	8.3	47	0	NM	91.50%	93.60%	NM
Shpitzer	55	NM	NM	10.5	58	0	NM	84.20%	89.60%	23
Suh	62	NM	NM	NM	36	0	NM	100%	NA	17.4
Shen ‘15	31.6	10	0	7.75	10	0	10	NA	NA	83.7
Shen ‘13	36.4	42	3	NM	0	45	11	97.78%	NA	34.7
Shen	35.4	9	1	13.4	0	10	5	NA	100%	43
Store	47.8	1	6	NM	7	0	7	71.40%	NA	55.2
Trignano	42.9	NM	NM	2–5.7	34	0	NM	76.47%	NA	1.5
Tsuchiya	42.9	52	0	NM	52	0	NM	88.59%	NA	65
Van Germet	60.2	46	0	NM	46	0	10	100%	61%	36.1
Virigin	59	NM	NM	NM	168	0	38	96.60%	75%	31
Vayvada	25.4	11	0	NM	5	0	3	100%	NA	29.3
Wang	29.1	10	0	NM	0	10	NM	100%	NA	(2–18)
Wei 1998	51.1	34	2	12	0	36	NM	93%	44%	14

Table 4 (*continued*)

Study	Mean Age	Type of Reconstruction		Defect size	Flap characteristics		Dental Implants	Flap Success rate	Patient Survival	Follow up
	(Years)	Primary	Secondary	(CM)	Single flap	Double flap	Ptn. received			(months)
Wei 2003	51.9	0	20	9.6	20	0	NM	90%	100%	22
Wei	51.1	27	0	6	12	15	NM	96.30%	NA	NM
Wolff	64	22	2	5.5–18	10	14	8	95.80%	NA	NM
Yilmaz	38	NM	NM	10–15 cm	13	0	4	100%	100%	NM
Zender	62	54	0	NA	54	0	NM	90%	NA	30

rehabilitation, including 360 osseointegrated dental implants. Interestingly, complications tended to be fewer in patients who received perioperative radiation and/or chemotherapy than patients who did not (Fig. 2).

3.5. Methodological quality assessment

There was a positive correlation between publication year and MINORS total score ($r = 0.5549$, $P < 0.0001$, CI 0.3693 to 0.6979). The R^2 value suggests that 30% of MINORS improvement over time could be predicted by year of study publication (Fig. 3a). The majority of studies had methodological limitations, with an average MINORS score of 9.14 and a wide range of 4–18. The following parameters were the most likely to receive a low score:

1. Prospective collection of data: the vast majority of the data was not collected according to an established protocol before the beginning of the study
2. Unbiased assessment of the study endpoint: evaluations were not blinded, and the rationale for non-blinding was not clearly stated
3. Prospective calculation of the study size: Power analysis was not done prior to starting the study
4. Contemporary groups (there were some historical comparisons, i.e. control and studied groups were not managed at the same time period)
5. Baseline equivalence groups; the comparative groups were not similar regarding the criteria other than the studied endpoints.
6. Adequate statistical analysis; some of the included studies have not reported the confidence interval nor relative risk.

The average MINORS methodology Score for each item and the total MINORS methodology score are given in Table 1. When MINORS total score results were analyzed in term of the type of flap (free flap vs double flap), (Radio-chemotherapy) and with respect to defect size (more than 8 cm vs. less than 8 cm), there are no significant statistical differences among the comparable groups (Fig. 3b).

3.6. Meta-analysis

For flap success, there were six studies with sufficient data to perform a meta-analysis (Fig. 4a). None of the 6 studies indicated a significant association between flap success and method of reconstruction (primary vs. secondary) using the odds ratio. The 6 studies yielded a total sample size of $n = 87$, with an overall estimated odds ratio of 0.686 (95% confidence interval, 0.156–3.018; $p = 0.618$), which also indicated no significant association between flap success and method of reconstruction. There was no indication of heterogeneity (Cochran's $Q = 3.95$, d.f. $= 5$, $p = 0.557$) or publication bias (results not shown) (Fig. 4a).

For flap-related complications, there were 12 studies with sufficient data to perform a meta-analysis. None of the 12 studies indicated a significant association between presence of flap-related complications and type of defect (lateral vs. anterior-lateral) using the odds ratio. The 12 studies yielded a total sample size of $n = 220$, with an overall estimated odds ratio of 0.695 (95% confidence interval, 0.322–1.498; $p = 0.353$), which also indicated no significant association between flap-related complications and the defect site. There was no indication of heterogeneity (Cochran's $Q = 11.11$, d.f. $= 11$, $p = 0.434$) or publication bias (results not shown) (Fig. 4b).

4. Discussion

The primary aim of this systematic review was to compare the success rates of vascularized fibula grafts between the primary and secondary mandibular reconstruction and to compare flap-related complications between lateral and antero-lateral mandibular defects. The secondary aim was to examine the correlation between the defect size and location with the VFG flap success. We hypothesized that VFG would be more successful in primary than secondary reconstruction. Based on meta-analysis, however, there was no statistically significant difference in flap success rate between primary and secondary reconstruction. Primary reconstruction of the mandible is preferred whenever possible, since it supposedly provides an immediate solution to the esthetic and functional deficit created by the tissue loss, providing the space and conditions necessary for rapid and complete oral and dental rehabilitation (Markowitz et al., 1994; Martin et al., 1994). However, primary reconstruction is not always possible, or advisable. For example, the likelihood of local recurrence of the original tumor, or peri-operative infection frequently makes delayed reconstruction a necessity (Lawson and Biller, 1982). The decision to employ primary versus secondary reconstruction is made based on multiple factors. Primary reconstruction would save the patient an additional surgical procedure, while employing the original micro-environment of the defect bed. It could, therefore, be the faster route to optimal rehabilitation (Markowitz et al., 1994; Martin et al., 1994). On the other hand, combining resection and reconstruction within the same surgical setting carries the possibility of missing residual tumor cells leading to tumor recurrence, and necessitating a reconstruction revision. Therefore, secondary reconstruction could provide the surgeon with time to ensure the healing of oral cavity, eradication of cancer cells and reduction of infection risk (Lawson and Biller, 1982).

There is also an ongoing debate concerning the optimal timing of surgical intervention related to the timing of radiation and chemotherapy in management of mandibular cancer, especially where radiation and/or chemotherapy are also necessary. Preoperative radio/chemotherapy was reported to increase the incidence of post-operative infection, with subsequent removal of alloplastic material and fixation plates (Ettl et al., 2010). On the other hand, post-operative irradiation showed a negative effect on bone regeneration, including graft incorporation and subsequent dental rehabilitation (Jacobsson et al., 1985). However, Irjala et al. revealed that preoperative radiation therapy did not affect the functional or the aesthetic outcome of microvascular flap reconstruction (Irjala

Table 5
Details about the mandibular defect site and fixation plate.

Study	Mandibular Defect site							Fixation plate
	L	C	LC	LCL	H	HC	HCL	Type
Ang	9	2	—	3	1	—	—	Reconstruction Plate
Antony	17	—	—	—	—	—	—	Reconstruction Plate
Avraham	Not Mentioned							Reconstruction Plate
Bahr	Not Mentioned							Mini-plate/Reconstruction Plate
Baron	—	—	2	2	—	1	—	Mini-plate (Ti)
Boyed	17	1	10	2	1	—	—	Reconstruction Plate
Bianchi	17/31	—	—	—	—	—	—	Mini-plate
Bianchi								— — —
Caballero	—	1	3	—	3	—	—	Reconstruction Plate (Ti) [1]
Chao	—	—	—	—	2	4	—	Reconstruction plate
Chaine	—	—	2	2	5	—	—	Mini-plate
Chang 1998	6	—	—	—	—	—	—	Reconstruction Plate
Chang 2010	Not Mentioned							Reconstruction Plate
Chana	Not Mentioned							Reconstruction Plate
Cheung 1994	—	1	5	4	—	1	1	Mini-plate
Cheng 2009	Not Mentioned							Reconstruction Plate
Coredio	37	48	—	—	65	—	—	Reconstruction Plate (Ti)
Crosby	1	—	—	4	5	—	1	Reconstruction Plate
Dean	4	1	3	—	3	—	—	Reconstruction Plate
Dermirkan	Not Mentioned							Reconstruction Plate
Disa et al., 1999		18	—	—	—	—	—	Mini-plate (Ti)
Fan	—	—	—	6	—	—	25	Reconstruction Plate (Ti)
Farwell								Locking Plate/THORP/Mini-plate
Ferrari	3	2	2	7	—	—	—	Reconstruction Plate
Ferri	7	1	2	10	5	1	3	Mini-plate
Fuijiki	29	—	19	12	—	—	—	—
Gabr	9	—	—	8	—	—	—	Reconstruction Plate
Gabr								
Gonzales	23	2	11	—	6	—	—	Mini-plate (26.2%)/Reconstruction Plate (73.8%)
Hakim	13	3	2	6	10	—	3	Mini-plate/Mini-screw
Haughey 1994	6	1	7	5	2	—	—	Reconstruction Plate (14)- Mini-plate (6)-Kirschner wires (1)
He	5	—	1	—	1	—	—	Reconstruction Plate
Head	94	57		—	—	—	—	Locking Plate/Mini-plate
Heller	36	11	—	—	—	—	—	Reconstruction Plate (Ti/SS)
Hidalgo 89	3	6	—	—	3	—	—	Mini-plate (11)/Interosseous wire (1)
Hidalgo 95	13	2	8	11	26	—	—	Mini-plate (96%)/Interosseous wire.
Inbal 2015	Not Mentioned							Reconstruction Plate
Irajala	Not Mentioned							Reconstruction Plate (Ti) 1/10
Jeng	Not Mentioned							NM
Jeng	Not Mentioned							NM
Knott	Not Mentioned							Leibinger Plate (LMRP)
Kim	Not Mentioned							NM
Kannan	Not Mentioned							NM
LI 2009	3	1	1	—	1	—	—	Mini-plate
Li	3	1	1	—	1	—	—	Mini-plate (Ti)
Lee	2	—	5	4	4	—	—	Mini-plate
Lee	8	—	6	—	8	—	—	Mini-plate (Resin stent)
Miyamoto	—	—		11	—		—	Mini-plate (Ti)
Nikolaos	5	2	9	7	—	—	—	Mini-plate
Nakayama	—	1	3	3	—	1	—	Mini-plate (Ti)
Ooi	16	1	5	3	5	—	—	Reconstruction Plate
Pelad	6	5	2	—	—	—	—	Mini-plate
Philips	Not Mentioned							Reconstruction Plate
Posch	Not Mentioned							Reconstruction Plate
Pogrel	Not Mentioned							Reconstruction Plate
Politi	Not Mentioned							Reconstruction Plate
Shan	Not Mentioned							Reconstruction Plate
Shen 2015	Not Mentioned							Reconstruction Plate
Shen 2013	18	2	8	3	14	—	—	Reconstruction Plate
Shen	2	—	4	—	4	—	—	Reconstruction Plate
Shpitzer	14	3	19	9	2	0	0	Reconstruction Plate (Ti), THORP, Mini-plate
Shpitzer	17	3	25	9	4	0	0	Reconstruction Plate (Ti)
Suh	Not Mentioned							Locking Plate
Serra	3	—	—	—	2	—	1	Reconstruction Plate (Ti)
Sakuraba	47	—	22	30	1	—	1	Reconstruction Plate (Ti)
Santamaria	3	1	3	—	1	1	2	Reconstruction Plate
Store	4	—	—	—	1	—	2	Reconstruction Plate
Trignano	Not Mentioned							Reconstruction Plate
Tsuchiya	Not Mentioned							Reconstruction Plate
Wang	—	—	—	—	10	—	—	Reconstruction Plate (Ti)
Wei 1998	Not Mentioned							Reconstruction Plate
Wei 2003	16	2	2	—	—	—	—	Reconstruction Plate
wei	6	—	—	1	10	10	—	Mini-plate/Reconstruction Plate/Interosseous wire.

Table 5 (*continued*)

Study	Mandibular Defect site							Fixation plate
	L	C	LC	LCL	H	HC	HCL	Type
Wolff	13	—	6	—	—	—	5	Mini-plate (Ti)
Van Germet	Not Mentioned							Reconstruction Plate
Vayvada	11	—	—	—	—	—	—	Reconstruction Plate
Virigin	Not Mentioned							Reconstruction Plate
Yilmaz	Not Mentioned							Reconstruction Plate
Zender et,al	35	_	19	_	_	_	_	Reconstruction Plate

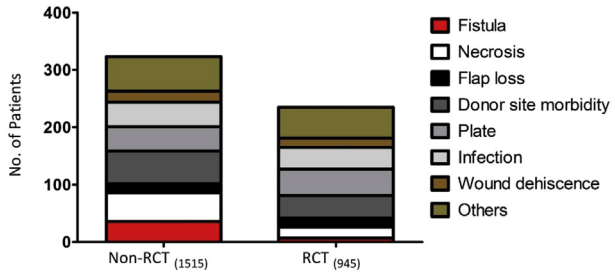

Fig. 2. Incidence of complications in patients who received radio-chemotherapy (RCT) and in those who did not receive (Non-RCT).

et al., 2012). He et al. concluded after his series of patients who had carcinoma for relatively short follow up period that the vascularized fibula flap can safely tolerate a 6,000-cGy dose of radiation post-operatively without developing serious complications (He et al., 2011). Our results showed that 25% of patients who received perioperative radiotherapy developed flap-related complications, which is slightly higher than those who did not.

Interestingly, the flap success in reconstruction of defect size more than 8 cm was higher than these less than 8 cm. Flap success in patient who received either double fibula flap or single flap was 98% and 92%, respectively. In 2015, a meta-analysis (Lonie et al., 2016) compared iliac to fibular flaps in mandibular reconstruction and concluded VFG should be considered more favorable in subtotal or total mandibular reconstruction, where length is required.

Anterior and antero-lateral mandibular defects have been considered challenging for reconstruction, due to the curvilinear outline of the mandible. According to the included studies, however, antero-lateral defects were not associated with higher rates of flap-related complications, compared to lateral defects. The majority of previous studies used Jewer et al.'s classification of mandibular defects based on its location (Jewer et al., 1989). The location of the defect is a major determinant of the reconstruction technique (Daniel, 1978). Based on an algorithm for mandibular reconstruction with osteofasciocutaneous free flaps (Papadopulos et al., 2008), the fibula has been advocated as the best option for

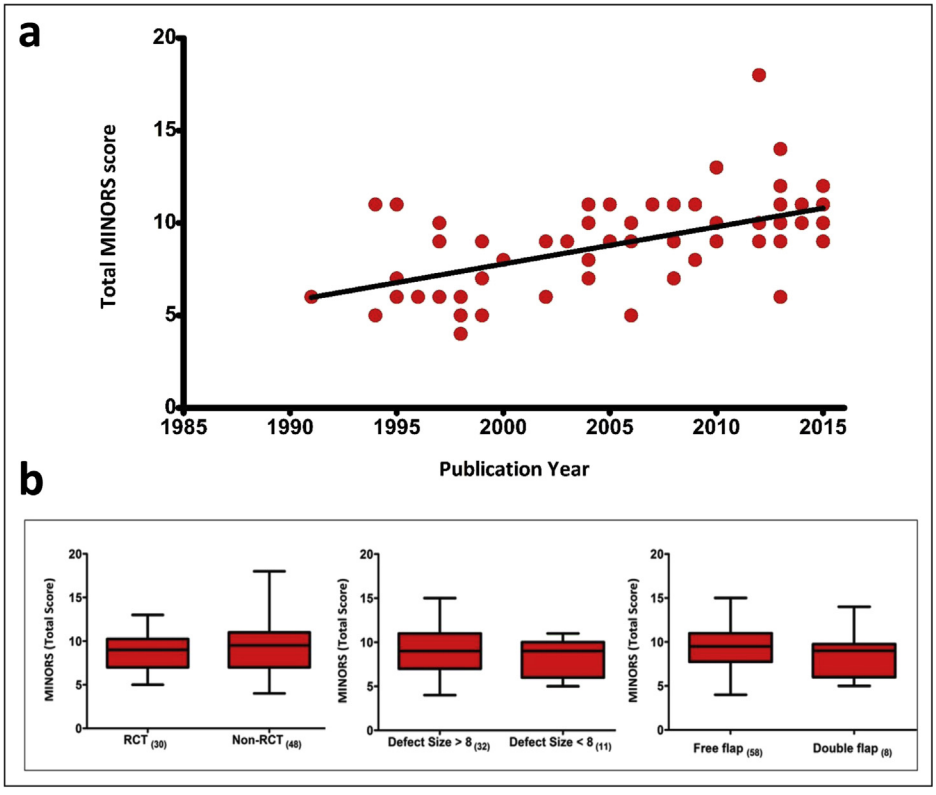

Fig. 3. a. Total methodological index for non-randomized studies (MINORS) score for studies used vascularized fibula graft for mandibular reconstruction plotted against publication year. **b.** Total methodological index for non-randomized studies (MINORS) score plotted against studies (a) that used radio-chemotherapy (RCT) for their patient perioperatively, (b) for studies performed reconstruction for defect more and less than 8 cm in size, and (c) Type of fibula flap used.

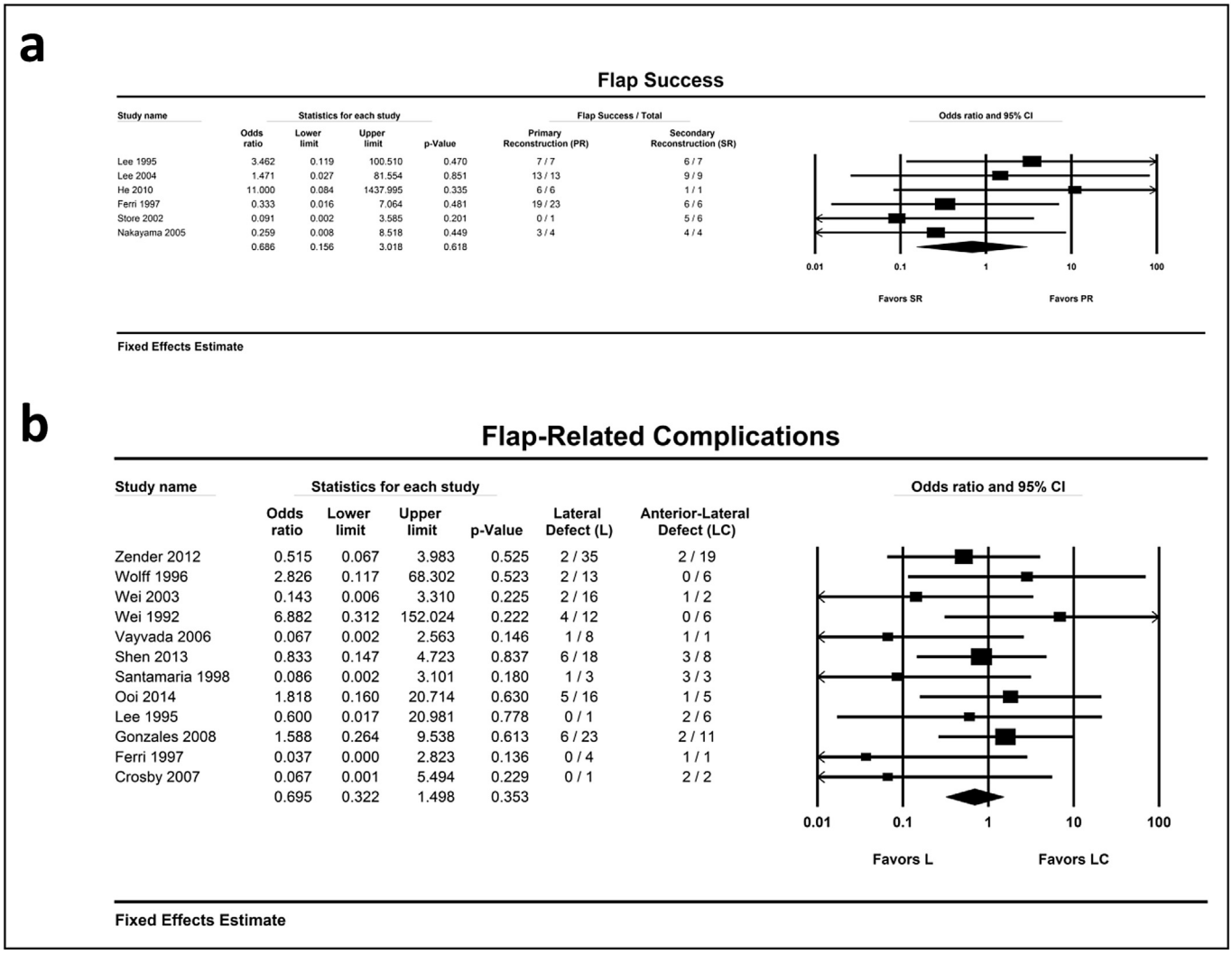

Fig. 4. a. Forest plot comparing the incidence of flap success between primary and secondary reconstruction. **b.** Forest plot comparing the incidence of flap-related complications between two different mandibular reconstruction sites (Lateral defect and Anterolateral defect).

reconstructing lateral and centro-lateral segments of the mandible, whether or not the soft tissues were also involved.

The outcome of reconstruction is expected to be influenced by the defect site and extents. Defects that involve the anterior curvature of the mandible present a significant mechanical challenge when chewing forces are considered. A commonly-cited classification of mandibular defects was introduced by Jewer and colleagues (Jewer et al., 1989), although several other classifications have also been suggested (David et al., 1988; Iizuka et al., 2005). According to Jewer's classification, the mandibular defects may be anterior, lateral, combined, or hemi-mandibular. Papadopulos et al. (Papadopulos et al., 2008) demonstrated that the VBF is the best reconstruction option for large lateral, as well as anterolateral defects. Literature showed that 50% of the anterolateral and 30% of lateral defects are actually reconstructed by fibula flap (Brown et al., 2016). Although the establishment of VBF as a commonly used option for these large defect to achieve functional and aesthetic restoration, the low diameter of the fibula presents a challenge for subsequent dental rehabilitation (Avraham et al., 2014). Several studies proposed the “double-barrel technique” to maximize the bony height to reconstruct the occlusal plane (He et al., 2011; Bahr et al., 1998). The vascularized double-barrel fibula showed positive outcomes of Osseointegration of dental implants and better reconstructive outcomes (He et al., 2011). However, segmentation of the fibula flap (up to 2 cm) to fit the mandibular contour may attenuate blood supply due to compression on the vascular pedicle (Glastonbury et al., 2014; Saponaro et al., 2015).

Many fixation techniques and hardware systems have been established for bridging mandibular defects with and without grafting (Jewer et al., 1989; Wang et al., 2013), most of which being made of titanium (Regev et al., 2010). A comprehensive discussion of the advantages and disadvantages of mini-plates in mandibular reconstruction has been introduced by Hidalgo and Pusic (2002). It is important to note that mini-plates have low risk of compromising the flap vascularization, in addition to their lower profile and easy and quick application procedure (Papadopulos et al., 2008). On the other hand, there is a risk of mobility and fracture of the mini-plates due to the extensive stresses present across the defect. On the other hand, Militsakh and his colleagues (Militsakh et al., 2004) reported low incidence of complications and superior stability with the use of locking reconstruction plates sized 2–2.4 mm as a fixation option after mandibular defects reconstruction. In 2007, Knott et al. (2007) demonstrated the effectiveness of LMRPs (locking mandibular reconstruction plate) used for

fixing vascularized bone grafts in mandibular reconstruction. However, it was still associated with 15% incidence of hardware-related complications that did not affect either the mandible continuity or dental occlusion.

Around twenty trials investigated the impact of dental rehabilitation on the post-reconstruction aesthetic function and dietary habit. A previous systematic review could not reach a firm conclusion on the overall impact of dental rehabilitation with implant-supported dental prostheses after mandibular reconstruction with VFG. In contrast, our study concluded that 41% of patients who received dental rehabilitation reported excellent aesthetic function thereafter, compared to 25% of patients who did not receive any dental rehabilitation. Also, 61% of patients who received dental rehabilitation reported being able to consume normal diet, compared to 44% in patients who did not. Moubayed et al. (2014) concluded that patients who had mandibular reconstruction with free fibular flap-experienced better quality of life and less depression symptoms.

A major challenge in the evaluation of outcome of mandibular reconstruction is the dissociation between surgical and functional success. Even in cases where the graft technique is successful, dental rehabilitation is still required to achieve complete functional and aesthetic restoration. Wu et al. (2008), and Teoh et al. (2005), described eligibility criteria for implant-based dental restoration after mandibular reconstruction, including tumor grade, stage, and the expected prognosis, residual tongue mobility, associated comorbidities that could influence the osseointegration and the quality and quantity of the reconstructed bone. Unfortunately, most vascularized flaps lack the minimally required dimensions for any meaningful restoration of dentition (Wells, 1996), with full-thickness iliac crest flaps providing a better alveolar ridge dimensions, while lacking the overall size and maneuverability necessary for large or anterolateral defects (Moscoso et al., 1994). In 2015, a meta-analysis comparing fibular and iliac flaps in mandibular reconstruction demonstrated that the average use of implants in iliac and fibular flaps was 4.15 and 3.11 implants per procedure respectively. However, there were not significant different in terms of aesthetic and functional outcomes of dental rehabilitation (Lonie et al., 2016). Multiple studies have reported high success rates of dental implants after mandibular reconstruction with vascularized fibula flaps (Bianchi et al., 2013; Hakim et al., 2015; Disa et al., 1999; Ferrari et al., 2013; Shen et al., 2015), albeit at high costs and additional surgical procedures. Pogrel et al. (1997) reported that only 20% of patient after reconstruction had implants. The high cost and/or lack of third party coverage has been reported as a major barrier to implant insertion and achieving ultimate dental rehabilitation after reconstruction (Peacock and Ji, 2017). Avraham et al. (2014) studied the effect of irradiation on dental implant placement. They reported that 80% of irradiated patients who went on to receive dental implants into grafted fibula flap did not experience any recipient site complication. On the other hand, Ferrari et al. (2013) compared the implant survival rate in the irradiated patients, prior placement and those who did not receive radiotherapy; and reported the rate to be 83.9% and 96.8% respectively. Furthermore, Hakim et al. (2015) reported that 10.4 % of 48 implants inserted into the 16 irradiated patients failed due to local infection and exposure. Further studies are needed to analyze the comprehensive long-term success of dental restoration between different techniques and conditions.

Current reconstruction techniques of the mandible with large segmental defects have many limitations and complications (Klotch et al., 1990). Vascularized osteocutaneous fibula flap can provide adequate stock of vascular bone with the shape and dimensions required for restoring the mandibular arch, as well as some skin cover (Hidalgo and Rekow, 1995; Urken et al., 1998). The fibula has been a favorable donor site over the ilium, scapula, and radius (Hidalgo, 1989; Lee et al., 1995). The fibula can be fashioned into a myriad of configurations, allowing better functional and esthetic outcomes (Lee et al., 1995; Disa et al., 1997). The high density and strength of fibula's cortex is convenient for installing dental implants (Zlotolow et al., 1992). Moreover, its location facilitates two-team approach and reduce operation time (Santamaria et al., 1998).

Donor-site morbidity following vascularized fibula flap has been studied in many clinical trials. Our review concluded that VFF was associated with very low incidence of donor site complications (Bodde et al., 2003; Babovic et al., 2000; Goodacre et al., 1990). Ling et al. (2013) demonstrated that patients donor site complications were much lower following the harvest of fibular than iliac crest vascularized. Biomechanical analysis revealed that there was no major instability after harvesting a fibular flap, except for a slight increase in knee flexion moment (Bozkurt et al., 2005).

The popularity of fibula flap in the mandibular reconstruction has been associated with increase in popularity of pre-operative computer-assisted planning technologies, such as computed tomographic imaging and virtual fabrication techniques (Valentini et al., 2005; Eckardt and Swennen, 2005). Pre-operative assessment of the 3D configuration of the defects become the standard for designing osteotomies, determining the most suitable flap, as well as the fixation method (Toro et al., 2007).

Despite concerns about the risk-benefit ratio, especially in pediatric patients (Crosby et al., 2008), the vascularized fibular flap remains a highly reliable reconstruction option (Li et al., 2009). Impact on subsequent mandibular growth potential could be reduced through the preservation of condylar cartilage (Genden, 2010). However, pediatric cases where the condyle must be included in the resection are likely to suffer deformity and malocclusion after reconstruction (Farkas et al., 1992). Further research is needed to establish a predictable reconstruction protocol in these cases.

The overall methodological quality of the included studies has shown a small improvement over the last two decades. The nature of these procedures makes randomization of patients, blinding, and adequate control almost unfeasible. Another major challenge is the large number of variables that make each patient condition unique. Finally, there has not been a consensus over a quantifiable measure of a reconstruction success. Careful examination of each study revealed inconsistencies in the use of terms such as flap success, patient satisfaction, dental rehabilitation, optimal esthetic outcome, etc., which is a limitation in these types of reviews. Our meta-analysis was limited by many confounding factors that may have influenced the flap success and its related complications after reconstruction. Multicentric, high-quality, trials are needed to further compare primary and secondary reconstruction, the impact of radio-chemotherapy, and the different features of the defect or the flap.

In conclusion, while this review and meta-analysis could not determine the optimal conditions for using a VFG in mandibular reconstruction, it provides valuable data for further reviews on the topic and can be used to guide future practice guidelines.

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