Clinical Outcomes of Vertical Distraction Osteogenesis for Dental Implantation: A Systematic Review and Meta-Analysis

Kai Zhao, DDS[1]/Feng Wang, DDS, MD, PhD[2]/Wei Huang, DDS, MS[2]/Yiqun Wu, DDS, MD, PhD[3]

Purpose: *The aim of this study was to evaluate the clinical outcomes of vertical distraction osteogenesis (VDO) for patients with vertically deficient alveolar ridges in terms of (1) the cumulative implant survival rate, (2) bone gain, (3) bone resorption before and after implant insertion, and (4) complications.* ***Materials and Methods:*** *An electronic search was conducted via MEDLINE (PubMed), EMBASE, and the Cochrane Library, complemented by manual searches, to identify eligible clinical studies of VDO before dental implantation. Two reviewers independently performed the study selection and data extraction. The implant survival rate, mean bone gain, and bone resorption amount, with 95% confidence intervals (CIs), were pooled separately. A random-effects model or fixed-effects model was chosen based on the heterogeneity. A funnel plot and Egger's test were performed to identify publication bias.* ***Results:*** *Of the 4,391 records after removal of duplicates, 113 full-text articles were obtained for further analysis, and 12 articles were ultimately included in the analysis. Two studies were defined as low quality. The estimated cumulative implant survival rate was 98.00% (95% CI: 96.02% to 99.40%), with a mean follow-up of 3.52 years. The bone gain was 7.92 mm (95% CI: 6.27 to 9.57 mm), with a range from 4 to 20 mm, and the level of bone relapse between the end of the distraction and the implant insertion was 0.97 mm (95% CI: 0.68 to 1.26 mm). The complication rate was high, with rates of 0.728 per site and 0.821 per patient. The most common major complication was basal bone fracture, with a rate of 2.27%, and the most common minor complication was displacement of the transport segments, with a rate of 16.71%.* ***Conclusion:*** *Vertical alveolar defects could be rehabilitated successfully with distraction osteogenesis, and the implant placed in the distraction sites showed a high cumulative survival rate. However, the high complication rate necessitates caution. Due to the observed heterogeneity, the results of this meta-analysis should be interpreted with caution.* Int J Oral Maxillofac Implants 2018;33:549–564. doi: 10.11607/jomi.6140

Keywords: *alveolar bone defects, bone augmentation, complications, dental implants, distraction osteogenesis, survival rate*

[1]Researcher, Second Dental Clinic, Department of Oral Implantology, Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai Key Laboratory of Stomatology, National Clinical Research Center of Stomatology, Shanghai, China.
[2]Associate Professor, Department of Oral Implantology, Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai Key Laboratory of Stomatology, National Clinical Research Center of Stomatology, Shanghai, China.
[3]Professor, Second Dental Clinic, Department of Oral Implantology, Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai Key Laboratory of Stomatology, National Clinical Research Center of Stomatology, Shanghai, China.

Correspondence to: Professor Yiqun Wu, Second Dental Clinic, Department of Oral Implantology, Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai Key Laboratory of Stomatology, National Clinical Research Center of Stomatology, No. 639 Zhizaoju Road, Shanghai, China 200011. Email: yiqunwu@hotmail.com

In the past few decades, dental implantation has become a widely accepted treatment for partially or completely edentulous patients, yielding reliable long-term outcomes.[1–7] However, alveolar bone deficiency caused by tooth extraction or traumatic or periodontal diseases has been a significant problem for implant dentistry. In particular, vertical alveolar deficiency, which is often associated with functional and esthetic problems, has become a great challenge for dental practitioners. Various surgical procedures have been proposed to solve these problems, including guided bone regeneration (GBR),[8–15] autogenous bone grafts (ABGs),[16–20] and vertical distraction osteogenesis (VDO).[21–25]

Successful correction of vertically deficient alveolar ridges using ABGs and vertical GBR has been reported in many clinical studies.[8–20] Autogenous bone grafting has been considered the gold standard due to its excellent osteogenic, osteoinductive, and osteoconductive capacities, but it is also associated with many

disadvantages.[18–20] The need to harvest native bone from intraoral and extraoral sites, with increased morbidity and long operating times, is considered the main disadvantage of ABGs.[17,26,27] Other shortcomings, such as bone resorption, wound dehiscence, infection, and the risk of nerve injury, have also been indicated in many studies.[16,18–20,28,29] As an alternative, vertical GBR has been used to correct vertical bone defects in numerous studies, and the clinical outcomes seem to be favorable.[8–15] However, the bone height achieved by vertical GBR is quite limited, and other disadvantages of vertical GBR, such as membrane exposure, bone resorption after membrane removal, and mucosal inflammation, have also been reported in several studies.[8,9,11,13–15,30]

Distraction osteogenesis, which was proposed by Codivilla in 1905[31] and developed by Ilizarov,[32–35] was originally mainly used in the orthopedic field. This approach was later applied to correct severe malformations in the maxillofacial field[36–38] and has been widely developed in recent decades to reconstruct vertically atrophied alveolar ridges.[21–25] Distraction osteogenesis seems to be reliable for the correction of vertical ridge defects, and numerous advantages have been described, such as the absence of a need for a secondary donor site, with reduced morbidity; the simultaneous formation of soft tissue with bone distraction; a low risk of infection; and shortened operating times.[22,39–42] However, VDO is a technique-sensitive procedure, and high complication rates have been reported in several studies.[43–45] Moreover, several potentially severe complications, such as inferior alveolar nerve injury, basal bone fracture, breakage of the distraction device, fracture of transport segments, an incorrect distraction vector, occlusal interference, bone resorption, and insufficient extension of the keratinized gingiva, have been reported in several clinical studies.[22–24,43–48] Therefore, the long-term outcomes of VDO have remained unpredictable.[43,44,48]

The aim of this systematic review was to evaluate the clinical prognosis of VDO based on *(1)* the cumulative implant survival rate, *(2)* the bone height achieved by VDO, *(3)* bone resorption before and after implant insertion, and *(4)* operative and postoperative complications.

MATERIALS AND METHODS

This systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement.[49] The following PICO (Participant, Intervention, Comparison, Outcome) question was addressed: In completely or partially edentulous patients with alveolar ridge deficiency, does VDO before implantation represent a reliable treatment in terms of the implant survival rate, bone gain, bone absorption, and occurrence of complications?

Search Strategy

To identify eligible studies for inclusion in the analysis, a systematic database search was conducted via MEDLINE (PubMed), EMBASE, and the Cochrane Library from January 1960 to October 2016. The search strategy is shown in Table 1. To prevent the omission of related studies, a complementary manual search of journal issues from January 2000 to October 2016 was also conducted for the following journals: *The International Journal of Oral & Maxillofacial Implants*, *Clinical Oral Implants Research*, *Clinical Implant Dentistry and Related Research*, *Journal of Clinical Periodontology*, *Journal of Periodontology*, *Journal of Oral and Maxillofacial Surgery*, *International Journal of Oral and Maxillofacial Surgery*, *Journal of Cranio-Maxillo-Facial Surgery*, *British Journal of Oral and Maxillofacial Surgery*, *Clinical Oral Investigations*, *Journal of Prosthetic Dentistry*, *International Journal of Prosthodontics and Restorative Dentistry*, *European Journal of Oral Implantology*, and *Journal of Oral Implantology*.

Study Selection

Judgment of the study selection was conducted independently by two reviewers (K.Z. and F.W.). For studies that appeared to meet the inclusion criteria or could not be judged based on titles and abstracts, full-text analysis was performed. Any discrepancy between the two reviewers was resolved by discussion. For disagreements that could not be resolved by the two reviewers, a third reviewer (Y.Q.W.) was consulted to reach a consensus. The inclusion criteria and exclusion criteria are shown in Table 2.

Data Extraction

Two reviewers (K.Z. and F.W.) independently extracted data from the included studies. The reviewers' degree of agreement was evaluated using the kappa test (Kappa = 0.82). Disagreements were resolved by discussion. The extracted data included the first author, year of publication, number of patients, follow-up time, distraction protocol (including the latency period, distraction rate, and consolidation time), implant number, bone gain amount, bone resorption from the end of distraction to implant insertion, implant survival rate, bone resorption after implant placement, and complications.

The VDO treatment usually encompassed three phases after surgery: a latency period, a distraction phase, and consolidation time. The latency period allows the healing of the wounds and preparation for the distraction procedure. During the distraction phase, the distraction devices are activated, and the two bone segments are slowly separated. The distraction rate is the distance that the distraction devices separate per day (usually from 0.5 to 1 mm/day), which determines the separation distance of two bone segments per day. A low distraction

Table 1 Search Strategy

MEDLINE	#1 (Jaw, Edentulous [MeSH]) OR (Jaw, Edentulous, Partially [MeSH]) OR (Missing tooth [all fields]) OR (Edentulous [all fields]) #2 (Alveolar Bone Loss [MeSH]) OR (Alveolar ridges atrophy [all fields]) OR (Alveolar bone defect* [all fields]) OR (Atrophic maxilla [tiab]) OR (Atrophic mandibular [tiab]) #3 (Dental Implants [MeSH]) OR (Dental Implantation [MeSH]) OR (Implant-supported denture* [all fields]) OR ((oral OR dental) implant* [all fields]) OR (endosseous implant* [all fields]) #4 (Osteogenesis, Distraction [MeSH]) OR (Distraction osteogenesis [all fields]) OR (Osteodistraction [all fields]) OR (Alveolar distraction [all fields]) OR (Vertical alveolar distraction [all fields]) OR (Alveolar ridge augmentation [MeSH]) OR (Vertical ridge augmentation [all fields]) OR (Bone augmentation [all fields]) #5 (Randomized controlled trial [pt]) OR (Controlled clinical trial [pt]) OR (Clinical trial) OR (Cohort study) OR (Case control study) (#1 OR #2) AND (#3 OR #4) AND #5 (3622)
EMBASE	#1 (edentulousness/exp) OR (missing and ('tooth'/exp OR tooth)) OR (edentulousness or (edentulous jaw)) #2 ('alveolar bone loss'/exp) OR (alveolar ridges atrophy) OR (alveolar bone defect*) OR (atrophic maxilla [tiab]) OR (atrophic mandibular [tiab]) #3 ('tooth implant'/exp) OR ('tooth implantation'/exp) OR ('implant-supported' and denture*) OR (endosseous and implant*) #4 ('distraction osteogenesis'/exp) OR (osteodistraction) OR (alveolar distraction) OR (vertical alveolar distraction) OR ('alveolar ridge augmentation'/exp) OR (vertical ridge augmentation) OR (bone augmentation) #5 (randomized controlled trial) OR (controlled clinical trial) OR (clinical trial) OR (cohort study) OR (case control study) (#1 OR #2) AND (#3 OR #4) AND #5 (1210)
Cochrane Library	#1 (Jaw, Edentulous explode all trees (MeSH)) OR (Jaw, Edentulous, Partially explode all trees (MeSH)) OR (missing tooth) OR (edentulous) #2 (Alveolar Bone Loss explode all trees (MeSH)) OR (Alveolar ridges atrophy) OR (Alveolar bone defect*) OR (Atrophic maxilla) OR (Atrophic mandibular) #3 (Dental implants explode all trees (MeSH)) OR (Dental implantation explode all trees (MeSH)) OR (Dental Prosthesis, implant-supported explode all trees (MeSH)) OR (Implant-supported denture*) OR (endosseous implant*) #4 (Osteogenesis, Distraction explode all trees (MeSH)) OR (Distraction osteogenesis) OR (Osteodistraction) OR (Alveolar distraction) OR (Vertical alveolar distraction) OR (alveolar ridge augmentation explode all trees (MeSH)) OR (Vertical ridge augmentation) OR (Bone augmentation) (#1 OR #2) AND (#3 OR #4) (745)

Table 2 Inclusion Criteria and Exclusion Criteria

Inclusion criteria	• Randomized or nonrandomized controlled trials, prospective cohort studies, retrospective cohort studies, case-control studies, and case series • Vertical distraction osteogenesis for maxillary or mandibular bone defects • Implant insertion after vertical distraction osteogenesis • Sufficient data for statistical analysis • At least 10 patients completed study and follow-up time of more than 1 year
Exclusion criteria	• Case reports • Animal studies • Horizontal distraction osteogenesis studies • No implant insertion after distraction osteogenesis • Bone defects related to congenital malformations • Bone defects related to tumor resection • Patient number less than 10 or follow-up time less than 1 year

rate is related to a slow separation velocity for two bone segments with a short separation distance, whereas a high distraction rate is related to a fast separation velocity with a long separation distance. After the distraction phase, the consolidation time (usually 3 to 6 months) allows the maturation of the newly formed bone between the separated bone segments.

Given that there is no consensus regarding the definition of the distraction rate, latency period, or consolidation time, stratification was performed. In this systematic review, a distraction rate of 1 mm/d, a latency period of 7 days, and a consolidation time of 3 months were considered as the boundaries. A distraction rate < 1 mm/d, a latency period < 7 days, and a consolidation time < 3 months were defined as a low distraction rate, short latency period, and short consolidation time, respectively. Accordingly, a distraction rate ≥ 1 mm/d, a latency period ≥ 7 days, and a consolidation time ≥ 3 months were defined as a high distraction rate, long latency period, and long consolidation time, respectively.

Quality Assessment

The quality assessment of the included studies was conducted independently by two reviewers (K.Z. and

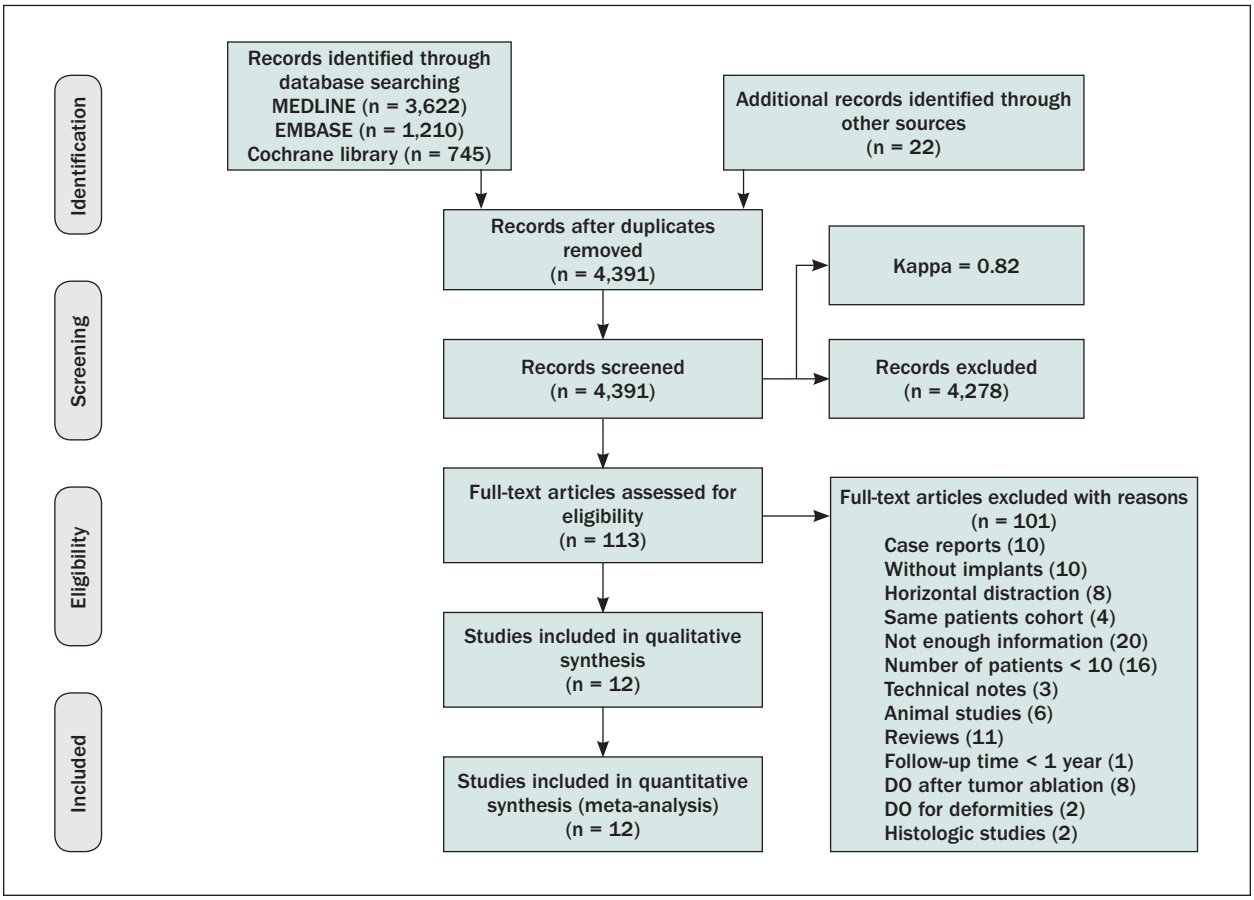

Fig 1 Flow diagram for the literature screening and study selection.

F.W.) based on the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.[50] This statement consists of a checklist of 22 items related to the titles; abstracts; and introduction, methods, results, and discussion sections of articles. Each item was scored from 0 to 1, with the total score for each study ranging from 0 to 22. Studies with a score < 11 (less than 50% of the maximum score) were considered poor quality.

Statistical Analysis

The measurement data, such as the bone gain and bone resorption amounts, are described as weighted means with 95% confidence intervals (CIs), and binary variables, such as the implant survival rate, are described as proportions with 95% CIs. The proportions and 95% CIs for outcomes were transformed using the variance-stabilizing Freeman-Tukey double arcsine method before pooling with a fixed- or random-effects model because the accuracy of the meta-analysis would be compromised if the proportion of binary data were too low or too high.[51,52] Heterogeneity among studies was evaluated with the Cochrane Q test and the I^2 statistic, which indicates the percentage of variation between studies due to heterogeneity rather than chance. $P < .05$ and $I^2 > 50\%$ represent significant heterogeneity.[53] If significant heterogeneity between the included studies was found, subgroup analysis and meta-regression were performed to identify the source of the heterogeneity, and a random-effects model was used. Funnel plots and Egger's test were also used to assess the publication bias. All meta-analysis procedures were conducted using R version 3.3.1 software (R Foundation).

RESULTS

Study Selection and Characteristics of the Included Studies

A total of 4,391 records were searched after the removal of duplicates (2,622 from MEDLINE, 1,210 from EMBASE, 745 from the Cochrane Library, and 22 additional records directly from journals and references). Next, 4,278 records were excluded based on the titles and abstracts. For the remaining 113 records, the full text was obtained and independently evaluated by the two reviewers (K.Z. and F.W.) based on the inclusion and exclusion criteria. In total, 101 articles were excluded for the reasons presented in Fig 1, resulting in the inclusion of 12 articles.[39,40,43–48,54–57]

Table 3 General Information on Included Studies

Study (year of publication)	Study type	No. of patients	Age of patients (y)	Follow-up time (y)	Edentulous area (complete or partial)	Latency time (d)	Distraction rate	Consolidation time (mo)
Faysal et al (2013)[39]	Prospective	18 (6 F/12 M)	51.5 (35–76)	1	Complete	7	0.5 mm/d	Group 1: 1.25 Group 2: 3.5
Marianetti et al (2013)[40]	Retrospective	27 (16 F/11 M)	18–75	2	Complete	6	0.8 mm/d	6
Enislidis et al (2005)[43]	Retrospective	37 (25 F/12 M)	41.8 (15–72)	2.96 (0.4–4.86)	Partial	8.2 (4–18)	0.9 mm/d (3 activations of 0.3 mm)	2.6
Wolvius et al (2007)[44]	Retrospective	20 (11 F/9 M)	36.8 (21–72)	1.4 (0.33–3.5)	Partial	7	0.9 mm/d (3 activations of 0.3 mm)	0.8–5.5
Pérez-Sayáns et al (2014)[45]	Retrospective	25 (14 F/11 M)	47.12 ± 9.2	4.54 (0.5–5)	NS	7	Maxilla: 0.5 mm/d Mandible: 1 mm/d	3
Chiapasco et al (2004)[46]	Prospective	28 (13 F/15 M)	39.2 (18–78)	2.83 (1.25–4.58)	Both complete and partial	7	1 mm/d (2 activations of 0.5 mm)	3
Zwetyenga et al (2012)[47]	Retrospective	37 (25 F/12 M)	51.7 (15–70)	5.33	Partial	7	1 mm/d	3
Ettl et al (2010)[48]	Retrospective	30	38.6	3.82	Partial	8.1 (6–13)	Track 1.0 mm: 0.9 mm/d (3 activations of 0.3 mm) Track 1.5 mm: 1 mm/d (2 activations of 0.5 mm)	4.5
Kim et al (2013)[54]	Retrospective	14 (5 F/9 M)	43.1	7.1 ± 1.7 (5.2–10.4)	Both complete and partial	6.2 (5–7)	1 mm/d (2 activations of 0.5 mm)	3.7
Sezer et al (2012)[55]	Prospective	10 (10 F)	46.7 ± 15.7	3	Partial	7	1 mm/d (2 activations of 0.5 mm)	4
Uckan et al (2007)[56]	Retrospective	21 (12 F/9 M)	37.9 (12–55)	Intraosseous group: 2.67 (0.67–6) Extraosseous group: 1.25 (0.5–2)	Partial	5	Extraosseous group: 1 mm/d (4 activations of 0.25 mm) Intraosseous group: 0.8 mm/d (2 activations of 0.4 mm)	2–3
Raghoebar et al (2008)[57]	Case series	46	NS	6 ± 0.86	Complete	5	1 mm/d	1–2

F = female; M = male; NS = not specified.

Among the 12 included studies, three[39,46,55] were prospective studies, eight[40,43–45,47,48,54,56] were retrospective studies, and the remaining study[57] was a case series. A total of 353 vertical distraction treatments were performed in 313 patients ranging in age from 18 to 78 years. A total of 64 treatments were performed in the maxilla, 261 treatments were performed in the mandible, and the remaining 28 treatments were not specified. A total of 983 implants were inserted, with a mean 3.14 implants per patient and 2.78 implants per site. The mean follow-up time in the included studies was 3.52 years, with a range from 1 to 7.1 years (Tables 3 and 4).

Quality Assessment

The mean score for the 12 included studies was 12.4, with a range from 9 to 16. Two included studies[43,56] were defined as poor quality due to a score less than 11. A lack of a prospective calculation of the study size and a lack of a statement about the potential bias were the most common shortcomings of the included studies. The details of the quality assessment are shown in Table 5.

Publication Bias

Begg's funnel plot was used to evaluate the publication bias of the included studies (Fig 2). The signs of symmetry in the funnel plot suggested an absence of publication bias. This finding was further supported by Egger's test, showing $t = -0.3984$, $P = .6987 > .05$, which indicated that there was no significant publication bias. However, publication bias could not be excluded completely due to the decreasing test efficiency caused by the limited number of included studies.

Implant Survival Rate

All 12 included studies provided data regarding the survival rate of the implants. Of all 983 implants placed, 28 were lost. The estimated overall cumulative survival

Table 4 Clinical Outcomes of Vertical Distraction Osteogenesis

Study (year of publication)	No. of surgical sites	Location of surgery	Type of device	No. of implants	Implant system
Faysal et al (2013)[39]	18	Mandible	MODUS (extraosseous)	36	Straumann
Marianetti et al (2013)[40]	27	Mandible	Martin (extraosseous)	189	NS
Enislidis et al (2005)[43]	45	Mandible	14 LEAD system (intraosseous); 31 Track 1.0 or 1.5 (extraosseous)	94	NS
Wolvius et al (2007)[44]	20	8 mandible 12 maxilla	Track 1.0 or 1.5, Martin (extraosseous)	63	NS
Pérez-Sayáns et al (2014)[45]	32	29 mandible 3 maxilla	24 Lead system (intraosseous); 8 MODUS 1.5/2.0 (extraosseous)	80	62 Straumann; 13 Frialoc; 5 Brånemark
Chiapasco et al (2004)[46]	28	19 mandible 9 maxilla	Track, Martin (extraosseous)	97	Brånemark; ITI; Biomet 3i; Frialit
Zwetyenga et al (2012)[47]	54	Mandible	NS	127	Brånemark
Ettl et al (2010)[48]	36	11 mandible 25 maxilla	Track Distractor (extraosseous)	82	2 Camlog; 7 Astra; 73 ITI
Kim et al (2013)[54]	14	12 mandible 2 maxilla	Track 1.5 (extraosseous)	41	NS
Sezer et al (2012)[55]	10	Mandible	MODUS ARS 1.5 V2 (extraosseous)	40	ITI
Uckan et al (2007)[56]	23	10 mandible 13 maxilla	13 LEAD system (intraosseous); 10 MODUS (extraosseous)	42	NS
Raghoebar et al (2008)[57]	46	Mandible	Groningen distraction device (intraosseous)	92	NS
Summary (95% CI)	353			983	

NS = not specified.

Table 5 Quality Assessment of Included Studies

Study (year of publication)	Items in STROBE														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Faysal et al (2013)[39]	1	1	1	1	1	0	0	1	0	0	1	1	0	0	1
Marianetti et al (2013)[40]	1	1	1	1	1	1	0	1	0	0	0	1	0	1	0
Enislidis et al (2005)[43]	1	1	1	0	1	1	0	0	0	0	0	0	0	1	0
Wolvius et al (2007)[44]	1	1	1	1	1	1	0	1	0	0	1	1	0	0	1
Pérez-Sayáns et al (2014)[45]	1	1	1	0	1	1	0	1	0	0	1	0	0	0	1
Chiapasco et al (2004)[46]	1	1	1	1	1	1	1	1	0	0	1	1	0	0	1
Zwetyenga et al (2012)[47]	1	1	1	0	0	1	1	1	0	0	0	0	1	0	1
Ettl et al (2010)[48]	1	1	1	1	1	1	0	1	0	0	1	1	0	0	1
Kim et al (2013)[54]	1	1	1	1	1	1	1	1	0	0	1	1	0	1	1
Sezer et al (2012)[55]	1	1	1	1	1	1	0	0	0	0	1	1	0	0	1
Uckan et al (2007)[56]	1	1	1	1	0	1	0	0	0	0	0	0	0	1	1
Raghoebar et al (2008)[57]	1	1	1	1	1	1	0	1	0	0	0	0	0	0	1

1 = Title and abstract; Introduction: 2 = background/rationale; 3 = objectives; Methods: 4 = study design; 5 = setting; 6 = participants; 7 = variables; 8 = data sources/measurement; 9 = bias; 10 = study size; 11 = quantitative variables; 12 = statistical methods; Results: 13 = participants; 14 = descriptive data; 15 = outcome data; 16 = main results; 17 = other analyses; Discussion: 18 = key results; 19 = limitations; 20 = interpretation; 21 = generalizability; Other information: 22 = funding.

Bone gain amount (mm)	Bone resorption after consolidation (mm)	Implant survival rate	Peri-implant bone resorption (mm)
Group 1: 6.968 ± 0.917; Group 2: 7.013 ± 0.900	Group 1: 0.832 ± 0.135; Group 2: 0.738 ± 0.135	94.4%	6 mo after prosthesis loading: Group 1: 1.380 ± 0.144; Group 2: 1.112 ± 0.144; After 1 year: Group 1: 1.590 ± 0.197; Group 2: 1.441 ± 0.197
10.5 (7–17)	NS	95.2%	After 1 year: 1.2 (0.5–1.7)
8.2 (5–15)	NS	95.7%	NS
Mesial point: 6.5 ± 0.459; Distal point: 6.1 ± 0.484	Mesial point: 1.2 ± 0.357; Distal point: 1.5 ± 0.408	98.4%	NS
6.15 (4–10) (intraosseous group: 5.74 ± 1.34); (extraosseous group: 8.36 ± 1.44)	NS	100%	NS
8.8 ± 3.5 (4–15)	0.3 ± 0.4	100%	1 y after prosthesis loading: 0.8 ± 0.4; After 2 y: 1.1 ± 0.5; After 3 y: 1.2 ± 0.4; After 4 y: 1.4 ± 0.4
11.648 ± 3.388	7 sites (all < 2 mm)	100%	NS
8.1 (5–14)	1.8 (0.4)	95.1%	50.4 mo after implant insertion: 3.5
8.4 ± 2.6	0.8 ± 0.3	97.3%	6 mo after prosthesis loading: 0.7 ± 0.2
7.2 ± 0.8	NS	100%	NS
11.6 (5–20)	NS	90.5%	NS
13.3 ± 0.7 (12–14)	1.357 ± 0.106	96.7%	NS
7.92 (6.27–9.57)	0.97 (0.68–1.26)	98.00% (96.02%–99.40%)	

Items in STROBE							
16	17	18	19	20	21	22	Total score
1	0	1	0	1	0	0	12
0	0	1	0	1	1	0	12
0	0	1	0	1	1	0	9
1	0	1	0	1	0	0	13
1	0	1	0	1	1	0	12
0	0	1	0	1	1	0	14
0	0	1	1	1	1	0	13
0	0	1	0	1	1	1	14
0	1	1	0	1	1	0	16
0	0	1	0	1	0	1	12
0	0	1	0	1	1	0	10
1	0	1	0	1	0	0	11

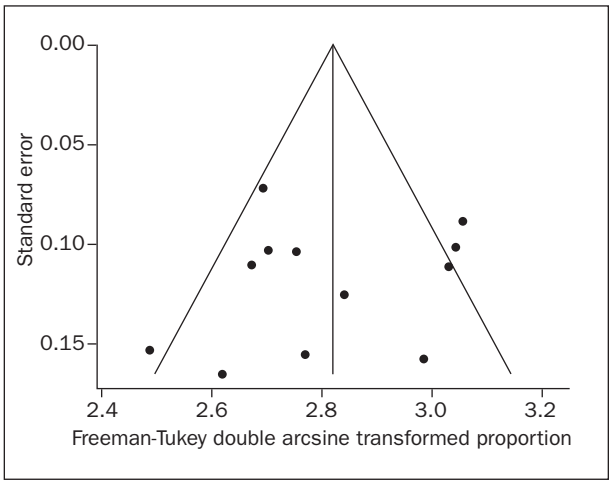

Fig 2 Funnel plot for meta-analysis of the included studies.

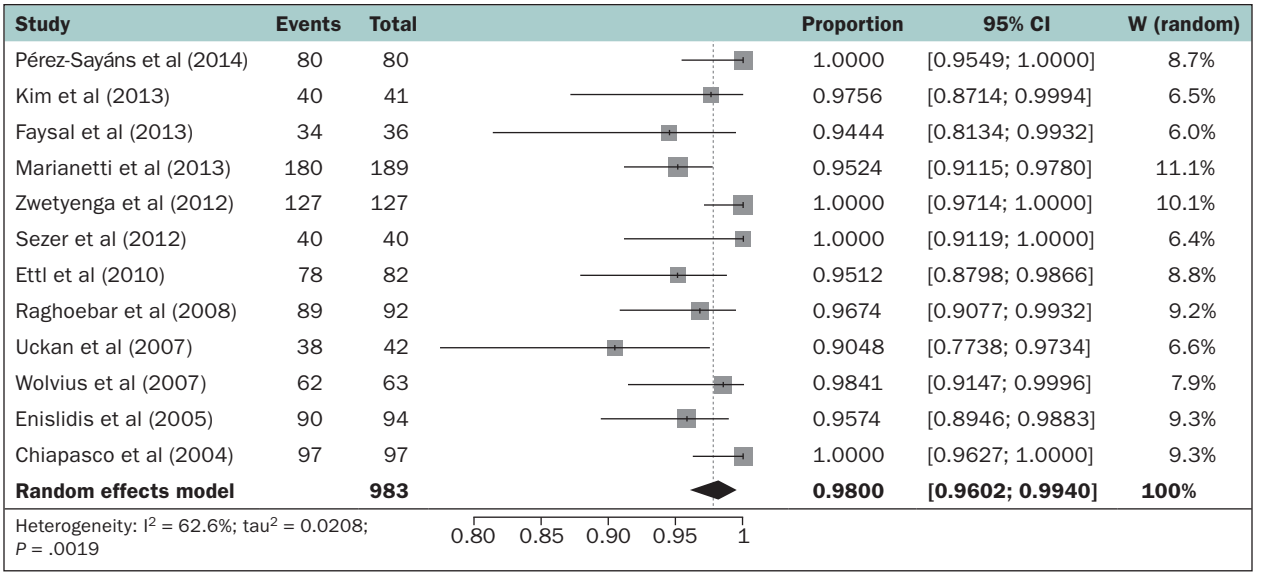

Fig 3 Forest plot of the estimated overall cumulative implant survival rate.

Table 6 Meta-regression of Included Studies

	Meta-regression coefficient	95% CI	*P* value
Distraction type (intraosseous vs extraosseous)	0.0306	−0.2193 to 0.2806	.8102
Latency time (low vs high)	0.1969	0.0012 to 0.3926	.0478
Consolidation time (short vs long)	0.2174	−0.0103 to 0.4452	.0614
Edentulous area (complete vs partial)	0.1042	−0.1377 to 0.3461	.3986
Study design (prospective vs nonprospective)	0.1212	−0.1328 to 0.3753	.3496

rate for the implants was 98.00% (95% CI: 96.02% to 99.40%), with a mean follow-up time of 3.52 years (Fig 3). Six included studies reported implants solely located in the mandible, with a pooled cumulative implant survival rate of 97.79%.[39,40,43,47,55,57] Another six studies reported implants placed in both the mandible and the maxilla, with a pooled cumulative implant survival rate of 98.17%.[44–46,48,54,56] No studies reported implants solely placed in the maxilla. The cumulative survival rate was 97.95% for implants placed solely in the anterior regions[39,43,47,57] and 98.28% for implants placed in both the anterior and the posterior regions.[40,43–48,54–56]

I^2 = 62.2% and *P* = .0019 indicated significant heterogeneity. Therefore, subgroup analysis was performed, and a random-effects model was used. In the subgroup analysis, the estimated cumulative implant survival rate in the intraosseous distractor group[45,56,57] was 97.16% (95% CI: 89.45% to 100%), which was lower than the rate of 97.96% (95% CI: 96.42% to 99.15%) in the extraosseous distractor group[39,40,44–46, 48,54–56]; however, this difference was not statistically significant (*P* = .974). With a long latency time,[39,43–48,55] the cumulative implant survival rate was 98.93% (95% CI: 96.90% to 99.98%), which was higher than that for a short latency time, namely, 95.70% (95% CI: 93.27% to 97.70%)[40,54,56,57]; this difference was statistically significant (*P* = .002). The implant survival rate for a long consolidation period[39,40,45–48,54,55] (98.97%, with 95% CI from 96.67% to 100%) was also higher than that for a short consolidation period[39,43,56,57] (95.71%, with 95% CI from 92.51% to 98.76%); this difference was also statistically significant (*P* = .009). However, no significant differences were identified in the subgroup analysis of the study design (prospective versus nonprospective, *P* = .178) or the subgroup of the edentulous area (complete versus partial, *P* = .101).

To further elucidate the source of heterogeneity, meta-regression was performed. Of the four meta-regression groups, only the latency time group was statistically significant and also considered to be a source of heterogeneity (*P* = .0478) (Table 6).

Bone Gain and Bone Resorption

All 12 included studies provided data about the bone gain level with VDO. However, four studies[40,43,48,56] only provided the means and ranges of the bone gain amount, and no standard deviation data or original data were available. Thus, these four studies were

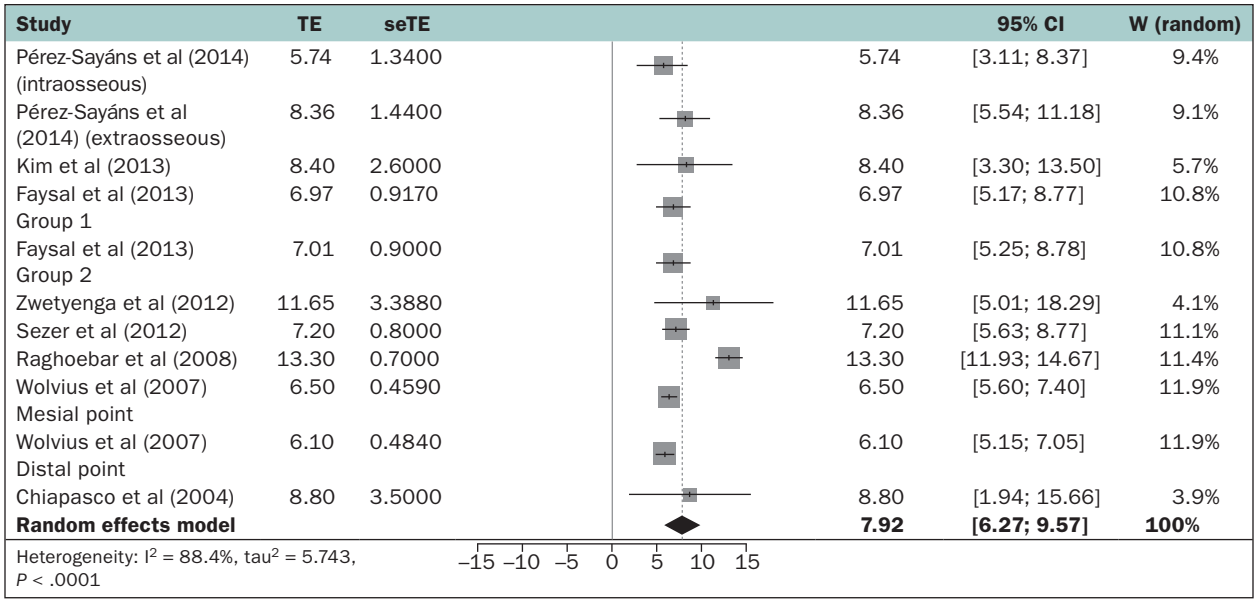

Fig 4 Forest plot of the estimated bone gain amount achieved by vertical distraction osteogenesis.

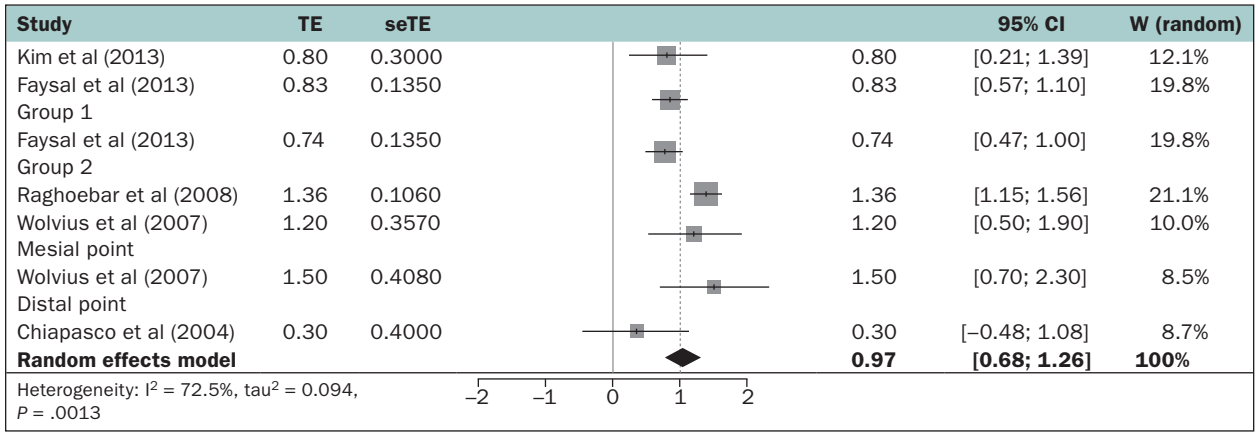

Fig 5 Forest plot of the estimated bone resorption amount.

not included in the statistical analysis. Based on the remaining eight studies, the pooled amount of bone gain was 7.92 mm (95% CI: 6.27 to 9.57 mm) (Fig 4). Six included studies[39,44–46,54,55] provided data about bone gain in the extraosseous distractor group. The pooled amount of bone gain for the extraosseous distractors was 6.64 mm (95% CI: 6.11 to 7.17 mm). Only two studies[45,57] provided bone gain data for the intraosseous distractor group: 5.74 mm (95% CI: 3.11 to 8.37 mm)[45] and 13.30 mm (95% CI: 11.93 to 14.67 mm).[57] No statistical analysis of bone gain was performed for the distractor group due to the limited number of included studies.

The pooled bone absorption amount for VDO from the end of distraction to the implant insertion was 0.97 mm (95% CI: 0.68 to 1.26 mm) based on the data provided by the five included studies[39,44,46,54,57] (Fig 5). Four of the included studies[39,44,46,54] provided data for the amount of bone absorption in the extraosseous distractor group. The pooled amount of bone resorption was 0.82 mm (95% CI: 0.65 to 0.98 mm). Only one study[57] provided bone resorption data for the intraosseous distractor group: 1.36 mm (95% CI: 1.15 to 1.56 mm). The pooled bone resorption amount was 0.98 mm (95% CI: 0.58 to 1.39 mm) for mandibular sites[39,57] and 0.94 mm (95% CI: 0.58 to 1.29 mm) for both maxillary and mandibular sites.[44,46,54] No data were available for the bone resorption amount for solely maxillary VDO sites. Moreover, one study reported a bone absorption amount of 1.357 ± 0.106 mm for anterior VDO sites, and four studies reported VDO in both anterior and posterior sites, with a pooled bone absorption amount of 0.82 mm (95% CI: 0.65 to 0.98 mm).[39,44,46,54,57]

Peri-implant Bone Resorption After Implant Insertion

The bone resorption amounts after implant insertion were only reported in five of the included studies.[39,40,46,48,54] In a prospective study,[46] peri-implant bone resorption was 0.8 ± 0.4 mm at 1 year after prosthesis loading, 1.1 ± 0.5 mm after 2 years, 1.2 ± 0.4 mm after 3 years, and 1.4 ± 0.4 mm after 4 years. In another prospective study,[39] peri-implant bone resorption was 1.380 ± 0.144 mm after 5 weeks and 1.112 ± 0.144 mm after 14 weeks in the consolidation time group 6 months after prosthesis loading. One year after prosthesis loading, the peri-implant bone resorption reached 1.590 ± 0.197 mm after 5 weeks and 1.441 ± 0.197 mm after 14 weeks in the consolidation time group. However, there were no significant differences between the two groups at any time. The peri-implant bone resorption amounts reported by the remaining studies were 0.7 ± 0.2 mm at 6 months after prosthesis loading,[54] 3.5 mm at 50.4 months after implant insertion,[48] and 1.2 mm (0.5 to 1.7 mm) 1 year after implant insertion.[40] No statistical analysis was performed due to the large heterogeneity of the available data.

Complications

In total, 257 complications of VDO (24 major complications and 233 minor complications) were observed at 353 surgical sites in 313 patients. The complication rate was 0.728 per site and 0.821 per patient (Table 7).

Major Complications

The most common major complication was basal bone fracture, with eight cases (2.27%) reported in five studies.[43,47,48,54,57] Four basal bone fractures occurred during the activation time, and the other four occurred during the postdistraction time. Several different remedial treatments were performed, including immediate osteosynthesis,[47] internal fixation using an intraoral approach,[43] replacement of the distraction device by another method that was not loaded to the fracture area,[57] and adjustment of the cap splint fixed to the mandibular arch with circumferential wiring.[48] The next most common major complications were transport segment fractures (five cases, 1.42%)[40,43,44,56] and device fractures (four cases, 1.13%).[43,48,54] Two fractures in the transport segment healed on their own, and the patients were then successfully rehabilitated with implantation.[40] One fracture was treated by vertical augmentation with bone and alloplastic materials covered by a membrane using an intraoral approach.[43] In another two fracture patients, the treatments were not reported.[44,56] All of the fractured devices were replaced with new distractors, and the whole treatment was ultimately completed. The remaining reported major complications were rare and included two (0.56%) severe misdirections of the segment, which required a secondary osteotomy for correction[47]; two (0.56%) permanent alveolar nerve paresthesia events[40,47]; one (0.28%) case of instability of the distractor[43]; and two (0.56%) mechanical problems related to the distraction device.[43]

Minor Complications

Lingual or palatal inclination of the transport segment was the most common minor complication and was observed in 59 cases (16.71%) reported in 10 studies.[40,43–48,54–56] Most cases were treated by manual repositioning, orthodontic appliance use, or minor additional grafting procedures at the time of implant insertion, which did not compromise the ultimate outcome. Another common minor complication was buccal bone defects[43–46,54,55] at the time of distractor removal, which commonly required a second bone graft procedure, such as GBR and autogenous bone grafting. Transient paresthesia of the nerve was another common minor complication (34 cases, 9.63%),[39,40,43,47,55,57] which disappeared spontaneously after several months, without influencing the implant placement or prosthesis loading. Other minor complications, such as soft tissue defects (21 cases, 5.95%),[45,48] occlusal interference of the rod (16 cases, 4.53%),[43,45,56] mucosal dehiscence (23 cases, 6.51%),[43,47,56,57] infection (12 cases, 3.40%),[40,43,47,55] and swelling (4 cases, 1.13%),[43] were also reported in several studies. The vast majority of minor complications were treated without great difficulties and did not compromise the ultimate results.

DISCUSSION

Vertical deficiency of the alveolar ridge has been a great challenge in dental implant practice. Although treatment protocols, such as GBR and autogenous bone grafting, have been applied to correct the defects, limitations are clearly present, including postsurgical bone resorption, limited augmentation amounts, and a lack of soft tissue coverage.[8–20] Distraction osteogenesis is a technique that allows the natural healing of human bone with gradual lengthening.[33,34] Since its first application for human dentoalveolar defect correction,[58] this technique has been widely used in recent decades to reconstruct vertical alveolar defects.[21–25,43–48,54–57] However, a high complication rate has been reported in several studies,[43–45,56] and the reliability of VDO has remained unpredictable.[43,44,48]

The present systematic review included 12 clinical studies of VDO. Three were prospective studies, eight were retrospective studies, and one was a case series. No randomized clinical trials were included, which is

Table 7 Complications of Vertical Distraction Osteogenesis

Study (year of publication)	Time and No. of complications that occurred				
	During surgery process	Latency period	Activation period	Consolidation period	Postdistraction period
Faysal et al (2013)[39]				Unilateral mental nerve paresthesia (4)	
Marianetti et al (2013)[40]			Sensory disturbance (6) Alteration of the distraction vector (2)	Segment fracture* (2) Infections (1)	Permanent paresthesia[a] (1)
Enislidis et al (2005)[43]		Dehiscence (2) Occlusal interference (1)	Dehiscence (3) Tilting of segment (4) Pain (3) Swelling (2) Hypoesthesia (2) Wrong direction (2) Fracture of basal bone[a] (1) Breakage of distractor[a] (1) Instability of distractor[a] (1) Other mechanical problem[a] (2)	Dehiscence (8) Hypoesthesia (3) Fracture of basal bone[a] (2) Pain (2) Swelling (2) Infection (2) Inflammation (1) Fracture of transport segment[a] (1)	Dehiscence (4) Infection (1) Hypoesthesia (2) Pain (1) Bone defects (11)
Wolvius et al (2007)[44]	Fracture of the transport segment[a] (1)		Lingual displacement of the transport segment (4) Palatal displacement of the transport segment (6)		Bone defects (10)
Pérez-Sayáns et al (2014)[45]			Lingual tilting of segments (6) Occlusal interference of the distractors (12)		Mucosa defects (8) Bone defects (20)
Chiapasco et al (2004)[46]			Lingual inclination (3) Palatal inclination (1)		Bone defect (1) Incomplete distraction (1)
Zwetyenga et al (2012)[47]		Transient paresthesia of the lower lip (8)	Major misdirection[a] (2) Minor misdirection (6) Basal bone fracture[a] (2) Exposure of distractors (4) Dehiscences (2)	Acute mucosa inflammation (6)	Permanent alveolar nerve paresthesia[a] (1)
Ettl et al (2010)[48]			Displacement of the transport segments (15)	Soft tissue dehiscences (2) Device fracture[a] (2) Fracture of mandible[a] (1)	Inadequate soft tissue extension (13)
Kim et al (2013)[54]			Lingual deviations of vector (2)	Basal bone fracture[a] (1) Device fracture[a] (1)	Horizontal bone defects (2)
Sezer et al (2012)[55]			Infection (1) Lingual inclination of the transport segment (1) Transient paresthesia (1)		Exposure of implant threads (1)
Uckan et al (2007)[56]	Intraoperative bleeding (1)		Lingual displacement of the transport segments (3) Palatal displacement of the transport segments (4) Rod interferences with the opposing arch (3)	Fracture of the transport segment[a] (1) Dehiscence of the soft tissue (1)	
Raghoebar et al (2008)[57]		Sensory disturbance (8)	Wound dehiscences (1)	Basal bone fracture[a] (1) Screw mobile (4)	Incomplete distraction (3)

[a]Major complication.

the greatest limitation of this systematic review. Studies examining bone defect cases caused by congenital malformations or tumor resection were excluded. Eight tumor resection patients and one congenital malformation patient in an included study[44] were also excluded from this review, whereas the data for the remaining patients were extracted. However, there were also five patients with tumor resection (1.6% of all included 313 patients) who could not be excluded because of the limited information provided by the authors[44,56]; this represents another limitation of the present study. Based on the limited information in this review, the cumulative implant survival rate for VDO was 98.00% (95% CI: 96.02% to 99.40%), with a mean follow-up time of 3.52 years, which is comparable to what has been observed for placement in native bone.[1–7,59,60] The cumulative survival rate was 97.79% for implants solely located in the mandible and 98.17% for implants placed in both the mandible and the maxilla. No data on implants solely placed

in the maxilla were provided in the included studies. Therefore, given the limited data available, no comparative analysis of implants placed in the mandible and maxilla could be performed. Based on the evidence presented here, it can be concluded that VDO implants placed in the mandible showed favorable outcomes, with a high cumulative survival rate, whereas the prognosis of VDO implants placed in the maxilla was not as certain as for the mandible and thus still needs to be assessed in clinical practice to reach a reliable conclusion. Further well-designed clinical studies with large sample sizes and long follow-up periods to evaluate VDO implants placed in the maxilla are also needed. A slightly lower implant survival rate was found for a short latency period and a short consolidation period; however, this outcome should be interpreted with caution because of confounding factors, such as patient characteristics, surgical protocols, and surgeons' skills, which could not be excluded. No publication bias was found based on Begg's funnel plot and Egger's test, but significant heterogeneity was identified. The latency time was considered to be a source of heterogeneity based on the subgroup and meta-regression analyses. However, the heterogeneity may have been derived from other sources, such as the patient characteristics, surgical practice, and the experience of the operators, among others. Analysis of these factors would be extremely difficult based on the present information. The lack of controlling of these confounding factors has limited the possibility to draw robust conclusions. Thus, the results of this meta-analysis should be interpreted with caution due to the observed heterogeneity. Additional high-quality studies with a strict epidemiologic design are needed in further research.

VDO is indicated in the following conditions: severe vertical alveolar deficiency of the edentulous range, an unfavorable implant-crown ratio caused by segmental alveolar defects,[61] vertical movement of ankylosed teeth or osseointegrated implants, bone lengthening of free fibular flaps,[62–65] and secondary treatment of placement for previously failed bone grafts.[66] Although distraction osteogenesis can be applied as a rescue treatment for a failed graft site, a higher complication rate could occur.[67] Therefore, it has been suggested that distraction osteogenesis should be the first line of treatment rather than a rescue procedure, if possible. In the following conditions, VDO is not recommended: an extremely atrophic mandible with a residual bone height of less than 5 mm[48,67]; a lack of a safe distance between the segment and vital anatomical structures, such as the inferior mandibular nerve/maxillary sinus/nasal floor and severe knife-edge ridges[42]; single tooth deficiency[44,47]; and combined horizontal and vertical deficiencies.[42]

Intraosseous and extraosseous distractors are the two types of devices mainly used in the authors' clinical practice. Extraosseous distractors are devices that are placed on the lateral surface of the alveolar bone subperiosteally and fixed to the basal bone using small screws. A rod is connected to the basal plate with an internal screw, and the transport segment moves apart from the basal bone when the internal screw is activated. Meanwhile, intraosseous distractors are often placed in such a way as to penetrate the transport segment vertically and are fixed to the basal bone using a microplate. Usually, an intraosseous distractor consists of three parts: a threaded rod, a transported plate, and a basal plate. The threaded rod penetrates the transported plate and bone segment in turn and connects to the basal plate, which is fixed to the basal bone. Similarly to what is performed for extraosseous distractors, the distraction procedure begins with activation of the threaded rod. In the present meta-analysis, the cumulative implant survival rate in the intraosseous group was 97.16%, which was slightly lower than the rate of 97.96% in the extraosseous group, but this difference was not statistically significant ($P = .974$). Compared with intraosseous distractors, extraosseous devices have a better capacity for vector control and thus might be more suitable for long transport segments.[45,56] However, occlusal interference occurs more frequently with extraosseous devices.[45,56] Moreover, patient tolerance is higher for intraosseous devices because of the smaller size and thinner rod, and the mucosa is also better preserved with intraosseous devices.[45,56] The choice of distractors should depend on the clinical conditions, which include the characteristic bone defects, patient acceptance, the distance to the opposing arch, and the experience of the surgeon.

Bone formation during distraction is influenced by the distraction rate. A distraction rate that is too low (lower than 0.5 mm/d) could cause premature union and prolong the distraction period; however, nonunion might occur if the rate is too quick (higher than 1.5 mm/d).[66,68] A distraction rate of 0.5 mm/d to 1 mm/d has been recommended in a number of studies.[67,69–71] The mean distraction rate in the present systematic review was 0.887 ± 0.203 mm/d, with a ridge from 0.5 to 1 mm/d and a high cumulative implant survival rate. These findings might indicate that a distraction rate from 0.5 to 1 mm/d is reliable in most situations. However, clinical choices regarding the distraction rate should also depend on the specified conditions. It has been suggested that in elderly people, a distraction rate of 1 mm/d results in a slight decrease in bone volume and a reduced vessel density. Thus, a lower distraction rate, namely, 0.5 mm/d, might be preferable to a distraction rate of 1 mm/d in the elderly.[72,73] Moreover, a lower rate has been recommended

for dense bone with low vascularity, horizontal distraction, and two-dimensional alveolar distraction.[66,67]

The length of the transport segments should span at least two implants[44,47] due to the higher complication rate expected for single-tooth transport segments and also the expectation of more bone resorption for short segments due to complicated screw fixation and devascularization.[24,74] However, if the transport segments are too long, then accurate control of the direction could also be difficult. Additional displacement of transport segments was found when these segments were longer than 20 mm.[48] Placement of two parallel intraosseous distractors or one extraosseous distractor rather than one intraosseous distractor has been recommended when the transport segments are longer than 2 cm.[45,56,75] For a narrow and long segment, intraosseous devices should not be used because the segment would be weakened by the rod insertion, and the risk of breakage would increase.[45,56] A minimum bone height of 4 to 5 mm for the transport bone fragment is necessary if use of intraosseous distractors is expected.[47,76,77]

One of the main problems associated with VDO is difficulty in accurately controlling the direction. In the present systematic review, displacement of the transport segments was the most common complication, occurring in 59 cases (16.7%) at 353 sites. Various methods were used to prevent and correct the vector problem, including orthodontic appliances,[44,78,79] bidirectional distractors,[80–82] two intraosseous distractors,[45,78,83] and provisional removable or fixed prosthodontic devices,[84] among others. An osteotomy line that diverges from the buccal sides to the lingual/palatal sides would be helpful to prevent segment tilting.[85] Although a high rate of vector tilting was found, it was easy to manage in most cases and did not compromise the ultimate outcomes.

Bone defects, including bone dehiscence and bone fenestration, were another common complication following segment displacement. To increase the predictability of implant placement after distraction osteogenesis, García García et al proposed a morphologic classification of postdistraction alveolar ridges[86]: type I for a wide alveolar rim and no bone defects; type II for a wide alveolar rim with buccal bone surface concavity; type III for a thin and narrow alveolar rim with buccal bone concavity; type IV for a bone bridge, without bone formation in the distraction chamber; and subcategory D for lingual or palatal displacement of the transport segments. Implant placement in type I–shaped bone results in an excellent prognosis with rare complications. The most frequent complications of implant placement in type II– and type III–shaped bone are bone fenestration and bone dehiscence, both of which require a secondary bone grafting procedure, such as GBR, or autogenous bone grafting. For type IV–shaped bone, fibrous tissue must be removed, and GBR should be performed before implant placement. In this systematic review, among 45 bone defect cases, 43 (95.56%) involved bone dehiscence or bone fenestration, each of which was associated with type II– and type III–shaped bone and was mainly treated by secondary bone grafting using bone chips, bone blocks, or alloplastic bone substitutes combined with reabsorbable collagen membranes.[43–46,54,55] Only two cases (4.44%) involved a "bone bridge" with bone defects at the distraction chamber sites, which were defined as type IV cases; both cases were treated by local augmentation with bone chips.[43]

Bone relapse during the consolidation period occurred frequently, with rates ranging from 0% to 25%.[39,40,43–48,54–57] In the present study, the mean bone height achieved was 7.92 mm, with 0.97 mm of bone relapse, and the mean bone resorption rate was 12.25% (95% CI: 8.59% to 15.91%). The pooled bone resorption amount was 0.98 mm (95% CI: 0.58 to 1.39 mm) for mandibular VDO sites, whereas no data were available for bone resorption at solely maxillary VDO sites. Therefore, no comparative analysis was performed, and further well-designed studies are needed, as mentioned earlier. Appropriate overcorrection was indicated to compensate for relapse. However, the amount of overcorrection was variable, including 15% to 20%,[44] 20%,[48] 20% to 25%,[39] 2 to 3 mm,[67] and 20% plus 0.32 to 0.52 mm.[74] Based on the present study, overcorrection of 10% to 15% might be suitable for most conditions, but this value also depends on the clinical situation. For sites that were treated with other surgical interventions within the previous 6 months, additional bone relapse at a rate up to 50% was reported after distraction osteogenesis. Therefore, at least 6 months are needed after any other surgery if VDO is to be performed.[87]

Nerve injury was another common complication of VDO. In total, 34 cases (9.63%) of transient paresthesia of the nerve and two cases (0.56%) of permanent alveolar nerve paresthesia were found in the present review. Intervention at a minimum of 5 to 7 mm above the inferior alveolar nerve is recommended to prevent injury to the inferior alveolar nerve.[24,43,67] Basal bone fractures were the most common major complication, with eight cases (2.27%) at 363 surgical sites. A minimal residual bone height of 5 mm was required to prevent basal bone fracture.[44,48] For an extremely atrophic jaw with a residual bone height less than 5 mm, VDO is not recommended unless a bone graft is conducted prior to the procedure.[48,68]

In conclusion, VDO can be successfully used to reconstruct vertical alveolar defects, with a high implant survival rate. A distraction rate of 0.5 to 1 mm/d might be suitable for most conditions, but clinical

decision-making should be based on the specific circumstances.

The implant survival rates for both intraosseous distractors and extraosseous distractors were comparably high. Whereas extraosseous distractors showed an excellent capacity for vector control, intraosseous distractors were preferable in terms of patient tolerance and mucosal preservation. The choice of distractor should depend on the clinical circumstances, including the characteristics of the bone defects, patient acceptance, and the experience of the surgeon.

At least two teeth are required to span bone defects for VDO. Intervention at a minimum of 5 to 7 mm above important anatomical structures is also indicated to prevent nerve injury. A minimum height of 4 to 5 mm and width of 4 mm is also recommended for the transport bone fragment to reduce resorption and complications.

Displacement of segments was the most common complication, but it was easily managed on most occasions, and various methods can be used effectively to prevent this complication. To compensate for bone relapse after distraction, an overcorrection of 10% to 15% might be suitable for most conditions, but clinical decision-making should also depend on the specific situation.

CONCLUSIONS

VDO can be used to correct vertical alveolar ridge defects successfully, with a high implant survival rate. However, a high complication rate is also observed. Therefore, VDO should be used with caution, and the clinical condition of the patient should be evaluated carefully. It should be stated that the results of this meta-analysis should be interpreted with caution due to the observed heterogeneity. Further well-designed clinical studies are needed.

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