Computer-assisted versus conventional freehand mandibular reconstruction with fibula free flap: a systematic review and meta-analysis

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ABSTRACT

Background

Computer-assisted mandibular reconstruction (CAMR) facilitates preoperative surgery simulation and transfers virtual plan to real operation. This systematic review and meta-analysis aimed to compare the accuracy, efficiency, postoperative complications and economic viability between CAMR and conventional freehand mandibular reconstruction (CFMR).

Methods

The PubMed, Embase, Cochrane Library and Google Scholar were searched up to November 2018. The accuracy, efficiency, postoperative complications and economic viability of CAMR compared to CFMR were systematically reviewed. Continuous and dichotomous data were pooled in mean difference (MD) (or standardized mean difference (SMD) if necessary) and odd ratio (OR), subsequently, with 95% confidence interval (CI).

Results

A total of 12 studies were included in the systematic review and data extracted from 11 of them were combined in meta-analysis. The accuracy of CAMR was better or equal to that of CFMR according to qualitative analysis, although the quantitative comparison from meta-analysis was excluded due to the diversity of measurements. As for efficiency, CAMR, when compared to CFMR, revealed a shorter ischemic time (MD: -34.81 min.; 95% Cl: -40.07 – -29.55) , reconstructive time (SMD: -2.48; 95% Cl: -3.16 – -1.80), total operative time (MD: -80.13 min.; 95% Cl: -96.72 – -63.53) and length of stay (MD: -2.27 day; 95% Cl: -4.04 – -0.49) . There was no difference of postoperative complication rate.

Conclusions

CAMR showed increased efficiency considering the reduced ischemic time, total operative time, reconstructive time and length of stay. However, the accuracy, reconstruction outcomes and perioperative cost should be further elucidated due to diverse measurements and the lack of included studies.

Computer-assisted versus conventional freehand mandibular reconstruction with fibula free flap: a systematic review and meta-analysis

INTRODUCTION

The fibula free flap (FFF) has become the workhorse for mandibular reconstruction.[1] The most prominent feature of FFF is the multiple segmentation of bone grafts, which can fully restore the curvature of mandible compared to other flaps. However, as the fibula is a linear bone, the major challenge of FFF is the bone segmentation and flap modelling.[2] Conventionally, surgeons did the segmentation and inset of fibula flap based on intraoperative scenes in a freehand approach. Therefore, the outcome of conventional freehand mandibular reconstruction (CFMR) mainly depends on the surgeon's skills, judgement in the moment, and trial-and-error in the operating room.[3]

The computer-assisted mandibular reconstruction (CAMR) was introduced with the development of computer-aided designing (CAD) and additive manufacturing (AM) technologies. CAMR facilitates surgery with the use of stereolithographic mandible model, cutting guides/surgical templates, and prebent/patient-specific surgical plate. Currently, there are multiple software available for CAD in mandibular reconstruction, such as Proplan/Surgicase CMF®, Mimics®, 3-Matic®, etc. The advantages of CAMR are especially significant in FFF reconstruction. The cutting guide enables precise mandibular resection to prevent violating the safe tumor margin, and also ensures that the osteotomy of fibula is performed at precise angles to maintain bone segments in engagement with each other at the recipient site. Then the fibula flap can be transferred to the recipient site using a positioning guide, or a prebent/patient-specific surgical plate, or surgical navigation. These patient-specific devices ensure the precise orientation of bone segments as planned and would enhance the accuracy of mandibular reconstruction.[4] Previous studies have indicated the benefits of CAMR in obtaining the accuracy of FFF reconstruction.[5-10] However, only a few studies have compared the accuracy of CAMR and CFMR, and no definite conclusions have been reached until now.[1,11-14]

Several studies have been published comparing CAMR with CFMR, which focused on different outcomes including the accuracy, efficiency, reconstruction outcomes, postoperative complications and economic viability. In assess the quality of existing evidence and provide insightful information to assist in the decision-making process, the strengths and weaknesses of CAMR and CFMR should be comprehensively evaluated. Therefore, we conducted a systematic review and meta-analysis to compare CAMR versus CFMR with FFF. The primary outcome was the accuracy of reconstruction. Secondary outcomes included the efficiency, reconstruction outcomes, postoperative complications and economic viability.

METHODS AND MATERIALS

The protocol of this systematic review and meta-analysis has been registered in Prospective Register of Systematic Review (PROSPERO No. CRD42018095189).

Search Strategy

A systematic literature search was conducted in PubMed, Embase and Cochrane Library for articles published up to November 2018. We employed different combinations of keywords from the following two domains: computer-assisted/aided and mandibular reconstruction. Meanwhile, a search for unpublished studies and those journals not indexed in the above databases was conducted in Google Scholar. Articles identified through reference list were also hand-searched. If articles with languages other than English were selected, the authors will be contacted for English translation. The full search strategy is presented in the document, **Supplemental Digital Content 1**, INSERT HYPER LINK.

Study Selection

Articles were initially screened based on the title and abstract. Full-texts were also reviewed to confirm the eligibility. The inclusion criteria: (1) included studies should be clinical trial, or observational study including both cohort and case-control study; (2) patients were diagnosed with benign or malignant tumor, osteomyelitis or osteonecrosis and indicated for mandibular reconstruction; (3) in the interventional or exposed group, patients underwent CAMR with FFF, using computer-assisted surgical planning and followed by transferring the surgical plan to actual surgery; (4) in the control group, patients underwent CFMR with FFF, without any computer-assisted planning and manufacturing; (5) study outcomes included one of the following parameters: the accuracy, efficiency, reconstruction outcomes, postoperative complications and economic viability. Meanwhile, studies were excluded to maintain homogeneity if patients were diagnosed with maxillofacial injury or dentofacial deformity. The studies without English translation will be also excluded. All studies were reviewed independently by two authors and in the event of disagreement between two authors, the inconsistencies were resolved through discussion.

Data Extraction

Two authors independently extracted data covering information: (1) demographic data of study population; (2) details of CAMR including imaging modality, virtual surgical plan, patient-specific devices; (3) methods and results of accuracy measurement; (4) efficiency parameters including reconstructive time, ischemic time, total operative time, length of stay; (5) reconstructive outcomes; (6) postoperative complications; (7) perioperative cost. The extracted data were checked by a third author.

Assessment of Risk of Bias in Included Studies

All studies were assessed using the Newcastle-Ottawa Scale.[20] The quality of studies was judged based on three broad perspectives: the selection of study groups (4 items), comparability of groups (1 item) and ascertainment of either the exposure or outcome of interest for case-control or cohort studies (3 items). Each study was awarded a maximum of one point for each item within the selection and exposure categories. A maximum of two points were awarded in the comparability category. Studies with a score of 6-9 points were defined as high methodological quality, while those with a score lower than 6 were low quality.

Data Analysis

The primary outcome was reconstruction accuracy. Secondary outcomes included the efficiency (reconstructive time, ischemic time, total operative time, length of stay), reconstruction outcomes, postoperative complications and perioperative cost. The reconstruction accuracy was defined as the deviations of anatomical landmarks between the virtual plan and actual surgical outcome. Reconstructive time was the time spent from the start of flap harvesting to the end of flap inset. Ischemic time was the duration since the flap's pedicle was divided to the time when anastomosis was done. Total operative time was the duration from surgery incision to wound closure. Length of stay was the postoperative inpatient days. Reconstruction outcomes of interest were postoperative facial appearance, mandibular movement, occlusion, nutrition and speech. Significant postoperative complications were flap loss, total/partial flap necrosis, and nonunion bone graft (no progress of bone healing between early and at least six-month postoperative imaging).

Studies reporting continuous and dichotomous outcomes were pooled in the meta-analysis. The pooled mean differences (MD) (or standardized mean difference (SMD) if indicated) and odds ratio (OR) with 95% CI were presented, and the p values of less than 0.05 were considered statistically significant. Substantial heterogeneity between studies was quantified using the chi2 (χ^2) with p value of < 0.10 or I^2 statistic of > 50%.[21] Due to the sparse data, either in case of low event rates or small study size, the fixed-effect models were performed to calculate the pooled outcome estimates.[22-23] Random-effect models were also performed as sensitivity analysis. All analyses were conducted in Review Manager (RevMan, version 5.3; the Cochrane Collaboration; Oxford, United Kingdom).

RESULTS

Study Selection

Four hundred and four articles were identified in PubMed, 246 articles in Embase, and 23 articles in Cochrane Library. After elimination of duplicated articles, 647 articles were left. Twenty-four articles were selected based on the title and abstract. These articles were read in full text. Subsequently, 12 articles were included in systematic review (Figure 1).

Study Characteristics

Study Design

This systematic review included 12 cohort studies published from 2015 to 2018, among which 4 studies were prospective [11,16,18,24] and 8 studies were retrospective. [1,12-14,15,17,19,30]

Participants

The total number of participants in CAMR and CFMR groups were 176 and 179, respectively. The diagnoses were malignant tumor (52.7%), mandibular benign neoplasms (25.6%), osteonecrosis (20%) and osteomyelitis (1.7%). Demographic data was shown in Table 1.

Intervention

All studies used spiral CT imaging for CAD. CAD was done to simulate mandibular osteotomy, [1,11-14,16-19,24] fibular osteotomy [1,11-14,16,17,19,24] and orientation of fibular segment at recipient site. [1,11-14,16-19,24] Additively manufactured devices (AMD) consisted of mandibular cutting guide, [1,11-14,16-19,24] fibular cutting guide, [1,11-14,16,17,19,24] fibular shaping guide,[14] stereolithography with pre-bent plate [13,14,17,18,24] and patient-specific surgical plates. [11,12,16,19,24] Two studies did not report the details of CAD and AMD.[15,30] Five studies reported the number of fibular segments. [12,13,16,17,24] Six studies mentioned the surgeon's experience. [1,12,17-19,30]

Analysis of the methodological quality

According to the Newcastle-Ottawa Scale, the quality of methodology was high in seven studies [1,12,13, 15,17,24,30] and low in five studies [11,14,16,18,19] (Table 2).

Primary outcome: accuracy

Five studies compared the accuracy of reconstruction between CAMR and CFMR.[1,11-14] The method of accuracy assessment was categorized as morphological evaluation of remnant mandible [1,12-14] and fibula segments.[11] Both methods compared pre-operative and post-operative images using specific anatomical landmarks. The accuracy of reconstruction was excluded from meta-analysis because each study used different angular/linear measurements and anatomical landmarks. Three studies identified significantly increased accuracy of reconstruction in CAMR compared to CFMR. Bao et al. reported significantly lower difference of both condylar and gonial shift in CAMR compared to CFMR.[14] Weitz et al. reported that the difference between preoperative and postoperative mandibular angle was significantly lower in CAMR.[1] De Maesschalack et al. measured linear and angular parameters of the affected and nonaffected mandibular sides, and only found the significant difference between two groups in axial angle of non-affected mandibular side.[12] Whereas the other two studies could not find any significant difference in accuracy between two techniques.[11, 13] Timing for postoperative imaging, methods for accuracy assessment and summarized results are shown in Table 3.

Secondary outcomes

Efficiency

Five studies evaluated ischemic time and showed a significantly shorter ischemic time in CAMR group.[13,14,17,19,30] Meta-analysis also demonstrated a significantly reduced ischemic time in CAMR group compared with CFMR (fixed-effect Inverse-Variance (I-V) model; MD: -34.81 min.; 95% Cl: -40.07 – -29.55; $p < 0.01$) (Figure 2A).

Reconstructive time was reported in three studies,[16,18,24] and all showed a significantly shorter reconstructive time in CAMR group. Meta-analysis demonstrated a significantly reduced reconstructive time for CAMR compared with CFMR (fixed-effect I-V model; SMD: -2.48; 95% Cl: -3.16 – -1.80; $p < 0.01$) (Figure 2B). The standardized mean difference was used in meta-analysis of reconstructive time because of diverse definition of the starting time point.

Of the seven studies evaluated total operative time,[14,15-19,30] four showed a significantly shorter total operative time in CAMR group,[14,16,17,30] whereas the other three showed non-significant difference.[15,18,19] Meta-analysis demonstrated a significantly shorter total operative time in CAMR group compared to CFMR (fixed-effect I-V model; MD: -80.13 min.; 95% Cl: -96.72 – -63.53; $p < 0.01$) (Figure 2C).

Of the six studies analyzed length of stay in hospital,[1,15,16,18,19,30] five reported no statistical difference between CAMR and CFMR groups.[1,15,18,19,30] In contrast, Tarsitano et al. showed a trend of shorter length of stay in CAMR group.[16] Meta-analysis demonstrated a significantly shorter length of stay in CAMR group compared with CFMR (fixed-effect I-V model; MD: -2.27 day; 95% Cl: -4.04 – -0.49; $p = 0.01$) (Figure 2D).

Reconstruction outcomes

Four studies reported reconstructive outcome of two groups (Table 4).[15,17,19,30] Wang et al. presented a greater number of patients had good facial appearance, regular diet and intelligible speech in CAMR group, but only good facial appearance was significantly different.[17] Ritschl et al. performed axiographic measurement for mandibular functional analysis and found non-significant difference between CAMR and CFMR groups.[15] Culié et al. also reported non-significant difference in enteral feeding time.[19] Bouchet et al. revealed better postoperative bite force of reconstructed side, mouth opening, right laterotrusion, protrusion and chewing satisfactory in CAMR group, but CFMR group showed superior aesthetic outcome.[30]

Postoperative complications

Eight studies showed postoperative complication rate.[1,11,13,14,16-19] Four studies presented no complication for both CAMR and CFMR.[11,13,14,17] Higher complication rates after CFMR were reported in 2 studies,[16,18] but the other 2 studies reported higher postoperative complication after CAMR.[1,19] Meta-analysis demonstrated similar postoperative complication rate (fixed-effect Mantel-Haenszel (M-H) model; OR: 0.54; 95% Cl: 0.16 – 1.85; $p = 0.33$) (Figure 3).

Economic viability

Two studies reported economic viability.[16,24] Zweifel et al. presented an extra cost of 1,231.50 USD in CAMR with pre-bent plate and 3,113.50 USD in CAMR with patient-specific surgical plate, compared to CFMR.[24] The calculation was based on total billable amount, money saved from operating time gain (47.50 USD per minute), and cost for surgical cutting guide, pre-bent/ patient-specific surgical plate and conventional plate. On the contrary, Tarsitano et al. demonstrated €450 cost saved in CAMR group compared to CFMR.[16] They calculated similarly to Zweifel et al.,[24] but money saved from operating time gain was based on €30 per minute.

DISCUSSION

This study is the first systematic review and meta-analysis comparing CAMR versus CFMR. For the primary outcome of reconstruction accuracy, although most studies reported improved accuracy in CAMR, this result remained inconclusive because meta-analysis was not done due to the diversity of measurements. For the secondary outcomes, our result confirmed that CAMR decreased the ischemic time, reconstructive time, total operative time and length of stay compared to CFMR, whereas reconstruction outcomes and postoperative complications were similar in both groups.

Accurate mandibular reconstruction is technically demanding.[25] In CAMR, the linear fibula is easily segmented and contoured to restore the neomandible by virtue of customized cutting guides. The incorporation of positioning guides and/or pre-bent/patient-specific surgical plates facilitates fibula segments molding, further contributing to the increased accuracy. On the contrary, CFMR mainly depends on the experience and skills of surgeons. In terms of measuring accuracy of CAMR, the general strategy is to measure the deviations of anatomical landmarks between the virtual plan and actual surgical outcome. Numerous anatomical landmarks have been employed to determine the deviations including the condyle, gonion, bone grafts and whole mandible. However, there is still a lack of standardized protocols of accuracy evaluation, severely restricting data interpretation and comparison among different studies. Regarding CFMR, accuracy evaluation usually compares postoperative and preoperative imaging since is no existing virtual plan. It is therefore prone to bias by directly comparing the accuracy outcomes of CAMR and CFMR. Meanwhile, in preoperative imaging, the anatomical distortion could disrupt measurements due to tumor occupancy. An alternative method is to mirror the contralateral healthy mandible for superimposition analysis, which provides relatively more reliable and reproducible outcomes. It should be well concerned that the postoperative stability of reconstructed mandible may also influence the accuracy outcomes. The postoperative stability could be affected by soft tissue contracture over time, for example, the condylar head can be significantly affected by the pterygomasseteric sling and surrounding soft tissue anchorage.[26] All these variables should be well standardized or controlled to retrieve comparable accuracy outcomes in future studies.

CAMR demonstrated a significant shorter reconstructive time compared to CFMR, which was predictable since CAMR simplified bone graft harvesting, molding, insertion and plate fixation. Similarly, CAMR allowed to perform fibula segmentation, alignment and fixation in the donor site before the vessel pedicle was divided, which could reduce the ischemic time. Meanwhile, the total operative time was significantly reduced in CAMR, which could be mainly attributed to the reduced reconstructive time. Interestingly, we noticed that CAMR saved more total operative time than reconstructive time, which might be due to the improved efficiency in mandibular resection using cutting guides. CAMR also resulted in a significantly shorter length of stay compared to CFMR. Although the increased ventilator dependence and operative time were significantly associated with prolonged length of stay in FFF reconstruction of head and neck defects,[31] the hospital stay was influenced by multiple factors, especially patients' comorbidities. As such, the relationship between reduced length of stay and CAMR was just specious reasoning. What's more, the statistically significant differences in ischemic time, reconstructive time, total operative time, and length of stay may or may not be clinically relevant, due to the lack of data on the minimal clinical important difference of these endpoints, which warrants future studies.

For the reconstruction outcomes and postoperative complications, there were no significant differences between CAMR and CFMR. Both groups restored mandibular continuity, providing adhesion anchor to surrounding soft tissue and muscles, resulting in comparable mandibular movement. However, the reconstruction outcome may be affected by postoperative radiotherapy.[28,29] Patients of both groups received nasogastric feeding for a similar period of time,[19] and resumed normal oral intake in most cases.[17] For aesthetic outcomes, both CAMR and CFMR achieved a good facial appearance.[17] However, regardless of the reconstruction accuracy, unpredictable soft tissue contractures due to scarring and radiotherapy can significantly affect facial appearance.

The major drawback of CAMR is the high expenses. Only two studies investigated the economic viability of CAMR compared to CFMR.[16,24] It deserves to be revealed how the saved operative time and length of stay can be translated to economic benefits before the cost performance of CAMR can be clarified. However, the expenses of operation theatre and inpatient services vary among different centers and countries. The health insurance coverage also varies in different areas. Therefore, the economic viability of CAMR remains an open question. Meanwhile, with the development and popularization of CAD and AM, the high expenses of CAMR would decrease in the near future, which would certainly promote the clinical application of CAMR.

Although CAMR can reduce operative time, surgeons have to spend additional time in preoperative planning. Like other new techniques, there is a learning curve for CAMR. Surgeons need certain clinical experiences to know how to mimics really surgery in the preoperative planning and to transfer the virtual plan to operation. The cost incurred in this additional planning time is hard to calculate. But on the other hand, the computer planning can serve as a training process for residents and junior surgeons to improve their understanding of complex reconstructive surgery, which is important for teaching hospitals.

There are some limitations to be addressed in our study. First, we could not identify any prospective, randomized controlled clinical trials comparing CAMR and CFMR. The number of included studies was also small, and five included studies were assessed as low quality in methodology. Thus, cautions should be taken not to overstating the conclusion. On the other hand, the lack of studies further highlights the rationale and necessity of the present systematic review and meta-analysis. Second, some confounding factors, including the surgeon experience and types of mandibular defects, were not well controlled in some included studies, which would inevitably produce bias. Although we have comprehensively assessed the risk of bias, we recommend all these factors should be well controlled in future studies. Last, we could not reach a definite conclusion concerning the accuracy of CAMR and CFMR, mainly due to the lack of consistent accuracy measurements in this outcome. Therefore, standardized methods of accuracy measurement in CAMR are warranted.

CONCLUSIONS

In summary, the accuracy of CAMR appears to be better or equal to that of CFMR, although meta-analysis was excluded due to the diversity of measurements. As for the efficiency, CAMR can decrease ischemic time, reconstructive time, total operative time and length of stay. The high expense has been an obstacle for CAMR, but the money saved from operating time gained may compensate the cost of designing and device. Prospective randomized controlled studies are required with standard measurement of outcome variables, especially for accuracy measurement.

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Table captions

Table 1. Demographic data of the included studies.

Table 2. Newcastle-Ottawa Scale to assess the methodological quality of the included studies.

Table 3. Parameters and results of mandibular reconstruction accuracy.

Table 4. Results of reconstruction outcome of included studies.

Figure legends

Fig. 1. Study flow diagram.

Fig. 2. Forest plots of comparison of efficiency between CAMR and CFMR: (A) ischemic time (B) reconstructive time (C) total operative time (D) length of stay.

Fig. 3. Forest plot of comparison of postoperative complication rate between CAMR and CFMR.

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Table 1. Demographic data of the included studies.

Table 1. Demographic data of the included studies.

Author Type of study	Year	Patient (n)		Mean age ± SD (range)		No. of Fibular segment (mean ± SD)		Surgeon's experience		Additively manufactured devices			
		CAMR	CFMR	CAMR	CFMR	CAMR	CFMR	CAMR	CFMR	Mandibular cutting guides	Fibular cutting guides	stereolithographic mandible with prebent plate	Patient-specific surgical plate
Ciocca et al [11] Prospective cohort study	2015	5	5	n/a	n/a	n/a	n/a	n/a	n/a	●	●		●
Gil et al [18] Prospective cohort study	2015	10	10	47 ± 14	64 ± 13	n/a	n/a	Same two teams of surgeon		●		●	
Zweifel et al [24] Prospective cohort study	2015	9	11	65.9 (55-78)	57.5 (48-70)	2.7	2.1	n/a	n/a	●	●	●	
Weitz et al [1] Retrospective cohort study	2016	24	26	55 ± 16	56 ± 13	n/a	n/a	Diverse surgeons		●	●	●	

Zhang et al [13] Retrospective cohort study	2016	8	14	35.5 (25-52)	35.9 (16-49)	3.38 ± 2.13	2.37 ± 1.74	n/a	n/a	●	●	●	
Tarsitano et al [16] Prospective cohort study	2016	20	20	48 (8-74)	59 (37-70)	3	2.4	n/a	n/a	●	●		●
Wang et al [17] Retrospective cohort study	2016	21	35	50.3 ± 4.2	53.6 ± 5.9	2.3 ± 0.6	2.7 ± 0.9	One surgical team		●	●	●	
Culié et al [19] Retrospective cohort study	2016	18	11	64.8 ± 8.9	60.6 ± 10.9	n/a	n/a	Three surgeons with more than 10 years' experience		●	●		●
De Maesschalck et al [12] Retrospective cohort study	2017	7	11	65.8 (45-79)	55.9 (42-62)	1.71	2.18	One surgeon	Three surgeons	●	●		●
Ritschl et al [15] Retrospective cohort study	2017	16	14	61.94 ± 11.64	63.07 ± 8.08	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Bao et al [14] Retrospective cohort study	2017	26	9	42.4 (17-64)	45.2 (29-61)	n/a	n/a	n/a	n/a	●	●	●	
Bouchet et al [30] Retrospective Cohort study	2018	12	13	59.25 ± 7.3	60.15 ± 12.6	n/a	n/a	Same senior surgeons		n/a	n/a	n/a	n/a

CAMR = computer-assisted mandibular reconstruction; CFMR = conventional freehand mandibular reconstruction; n/a = not available

Table 2. Newcastle-Ottawa Scale to assess the methodological quality of the included studies.

Table 2 Newcastle-Ottawa Scale to assess the methodological quality of the included studies.

Study	Selection	Comparability	Outcome	Score (max 9)
Ciocca et al [11]	2	0	1	3
Gil et al [18]	3	0	2	5
Zweifel et al [24]	3	1	3	7
Weitz et al [1]	3	0	3	6
Zhang et al [13]	3	1	3	7
Tarsitano et al [16]	2	1	1	4
Wang et al [17]	3	1	3	7
Culié et al [19]	2	0	1	3
De Maesschalck et al [12]	3	1	3	7
Ritschl et al [15]	3	0	3	6
Bao et al [14]	3	0	2	5
Bouchet et al [30]	3	1	3	7

Table 3. Parameters and results of mandibular reconstruction accuracy.

Table 3. Parameters and results of mandibular reconstruction accuracy

Author	Follow-up period of postoperative CT	Parameters for the accuracy assessment	Results of reconstruction accuracy between CAMR and CFMR (Difference between preoperative virtual plan and postoperative outcomes)
Ciocca et al [11]	n/a	1) Lateral shift of lower mesial point of FS	1.36 (CAMR), 4.11 (CFMR)
		2) Lateral shift of lower distal point of FS	2.22 (CAMR), 4.10 (CFMR)
		3) Vertical shift of lower mesial point of FS	2.93 (CAMR), 2.17 (CFMR)
		4) Vertical shift of lower distal point of FS	2.90 (CAMR), 2.11 (CFMR)
Weitz et al [1]	n/a	1) Gonial angle (°)	4.5° (CAMR), 11.5° (CFMR)*
		2) Distance from the angle to the midline (mm)	5 ± 3.9 (CAMR), 8.2 ± 7.1 (CFMR)
Zhang et al [13]	within 2 weeks	1) Intercondylar distance (mm)	2.97 ± 1.71 (CAMR), 4.12 ± 3.8 (CFMR)
		2) Intergonial angle distance (mm)	2.96 ± 1.85 (CAMR), 4.45 ± 3.06 (CFMR)
		3) Anteroposterior distance analysis (mm)	4.27 ± 3.62 (CAMR), 5.07 ± 5.47(CFMR)
		4) Gonial angle (°)	3.22 ± 3.14 (CAMR), 4.81 ± 4.7 (CFMR)

De Maesschalck, et al [12]	at least 3 months		Affected side	Contralateral side
		1) Distance between condylion and gonion (mm)	4.8 ± 4.5 (CAMR), 3.4 ± 3.7 (CFMR)	0.4 ± 0.6 (CAMR), 0.7 ± 1.4 (CFMR)
		2) Distance between gonion and the parasymphysis (mm)	5.9 ± 4.6 (CAMR), 6.1 ± 4.1 (CFMR)	2.7 ± 4.0 (CAMR), 4.1 ± 5.1 (CFMR)
		3) Distance between gonion and gnathion (mm)	5.3 ± 4.6 (CAMR), 4.8 ± 3.9 (CFMR)	3.2 ± 4.6 (CAMR), 4.6 ± 5.6 (CFMR)
		4) Angle formed by the plane passing through the gonion and the parasymphysis and a midsagittal plane (°)	1.8 ± 1.1 (CAMR), 3.4 ± 4.7 (CFMR)	1.0 ± 0.9 (CAMR), 2.9 ± 2.3 (CFMR)*
		5) Angle formed by the plane passing through the gonion and the parasymhysis and the plane passing through the gonion and condylion (°)	4.2 ± 2.6 (CAMR), 4.5 ± 3.5 (CFMR)	0.4 ± 0.5 (CAMR), 2.2 ± 3.0 (CFMR)
Bao et al [14]	3 months	1) Condylar shift (mm)	4.46 ± 2.12 (CAMR), 8.96 ± 1.01 (CFMR)*	
		2) Gonion shift (mm)	4.57 ± 1.66 (CAMR), 8.99 ± 1.48 (CFMR)*	

FS = fibular segment; CAMR = computer-assisted surgery; CFMR = conventional freehand surgery; n/a = not available

* Statistically significant difference (p <0.05)

Table 4. Results of reconstruction outcome of included studies.

Table 4. Results of reconstruction outcome of included studies

Author	Reconstruction outcome
Wang et al [17]	Good facial appearance (%): 95.2 (CAMR), 77.1 (CFMR)*
	Regular diet (%): 100 (CAMR), 85.7 (CFMR)
	Intelligible speech (%): 100 (CAMR), 97.1 (CFMR)
Culié et al [19]	Enteral feeding time (day): 24 ± 13 (CAMR), 31 ± 17 (CFMR)
Ritschl et al [15]	Mouth opening (mm): 30.81 ± 11.79 (CAMR), 28.36 ± 9.4 (CFMR)
	Protrusion (mm): 6.31 ± 2.49 (CAMR), 6.36 ± 1.59 (CFMR)
	Laterotrusion right (mm): 6.69 ± 37 (CAMR), 4.86 ± 2.98 (CFMR)
	Laterotrusion left (mm): 6.63 ± 2.78 (CAMR), 5.5 ± 2.79 (CFMR)
	Deviaton right (mm): 2.38 ± 2.55 (CAMR), 2.71 ± 1.54 (CFMR)
	Deviation left (mm): 1.75 ± 1.29 (CAMR), 2.21 ± 2.12 (CFMR)
	Deflexion right (mm): 0.94 ± 1.34 (CAMR), 1.5 ± 2.28 (CFMR)
	Deflexion left (mm): 1.5 ± 2.88 (CAMR), 2.21 ± 2.29 (CFMR)
Bouchet et al [30]	*Functional outcome:*
	Post-operative bite force of reconstructed side (Newton): 218.2 (CAMR), 189.2 (CFMR)
	Post-operative bite force of non-reconstructed side (Newton): 344.3 (CAMR), 325.1 (CFMR)
	Masticatory ability for solid foods**: 3.6 (CAMR), 3.8 (CFMR)
	Mouth opening (mm): 35.5 (CAMR), 31.1 (CFMR)

Laterotrusion right (mm): 3.0 (CAMR), 2.5 (CFMR)
Laterotrusion left (mm): 2.3 (CAMR), 2.4 (CFMR)
Protrusion (mm): 2.1 (CAMR), 1.8 (CFMR)
Subjective eating satisfaction (AVS): 6.3 (CAMR), 6.8 (CFMR)
Subjective chewing satisfaction (AVS): 5.3 (CAMR), 4.9 (CFMR)
Aesthetic outcome:
Midline chin deviation (mm): 3.5 (CAMR), 4.7 (CFMR)
Subjective aesthetic satisfaction (AVS): 6.9 (CAMR), 7.3 (CFMR)
Subjective Social activity satisfaction (AVS): 8.3 (CAMR), 8.6 (CFMR)

CAMR = computer-assisted mandibular reconstruction; CFMR = conventional freehand mandibular reconstruction; AVS = analogue visual scale

* Statistically significant difference (*p* <0.05)

** Masticatory ability for solid foods was evaluated using a modification of the method proposed by Yamamoto et al.[32] which foods were ranked by consistency on a scale ranging from very soft (category 1) to very hard (category 6).

Figure 1 Click here to access/download;Figure;Figure 1.final.tif

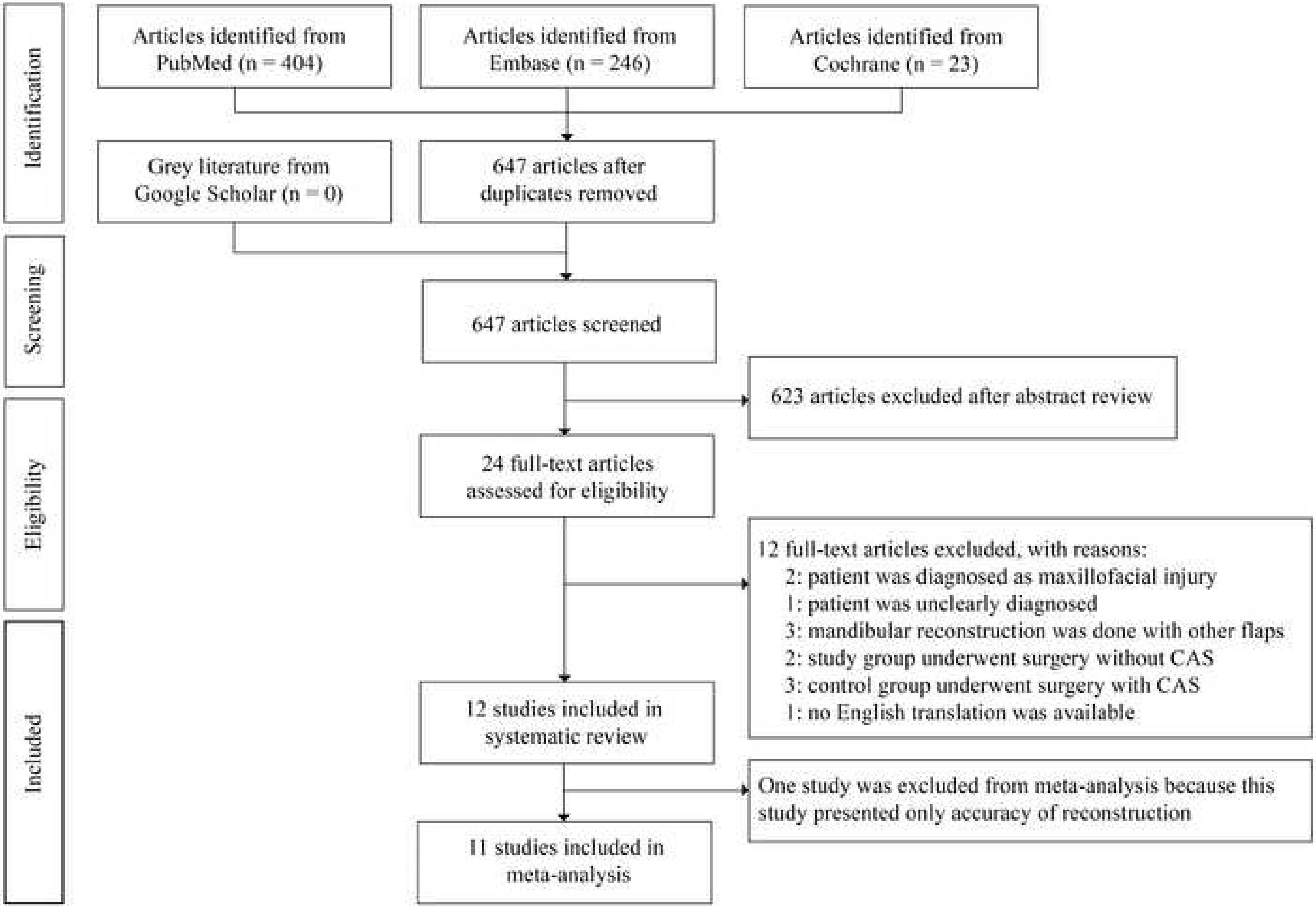
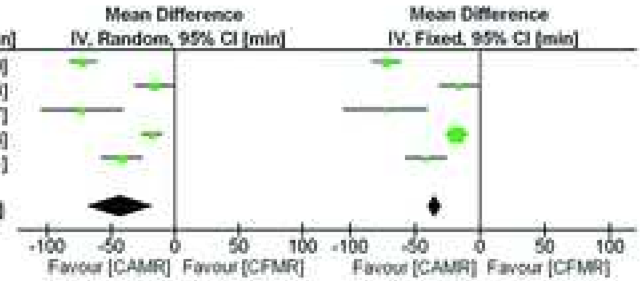


Figure 2

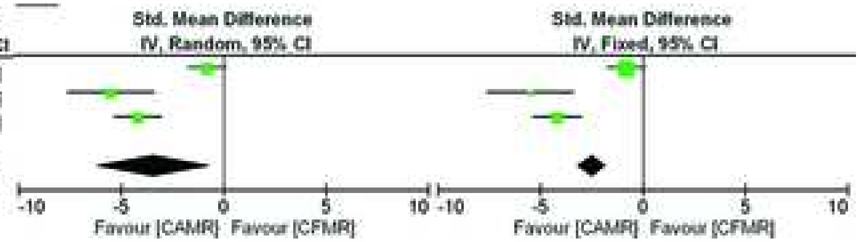
Study or Subgroup	CAMR Mean [min]	CAMR SD [min]	CAMR Total	CFMR Mean [min]	CFMR SD [min]	CFMR Total	Weight	Mean Difference IV, Random, 95% CI [min]	Weight	Mean Difference IV, Fixed, 95% CI [min]
Bao et al.	87.38	17.83	26	159.44	12.71	9	21.2%	-72.06 [-82.83, -61.29]	23.9%	-72.06 [-82.83, -61.29]
Bouchet et al	71.66	20.2	12	87.92	17.53	13	20.5%	-16.26 [-31.14, -1.38]	12.5%	-16.26 [-31.14, -1.38]
Culie et al.	98	45	18	171	41	11	16.5%	-73.00 [-104.93, -41.07]	2.7%	-73.00 [-104.93, -41.07]
Wang et al.	45	13	21	63	15	35	21.6%	-18.00 [-25.46, -10.54]	49.8%	-18.00 [-25.46, -10.54]
Zhang et al	52.53	13.14	8	94.18	24.75	14	20.3%	-41.65 [-57.49, -25.81]	11.0%	-41.65 [-57.49, -25.81]
Total (95% CI)			85			82	100.0%	-42.95 [-68.90, -17.00]	100.0%	-34.81 [-40.07, -29.55]

Heterogeneity: Tau² = 797.99; Chi² = 77.68, df = 4 (P < 0.00001); I² = 95%
Test for overall effect: Z = 3.24 (P = 0.001) Random effect
Test for overall effect: Z = 12.96 (P < 0.00001) Fixed effect



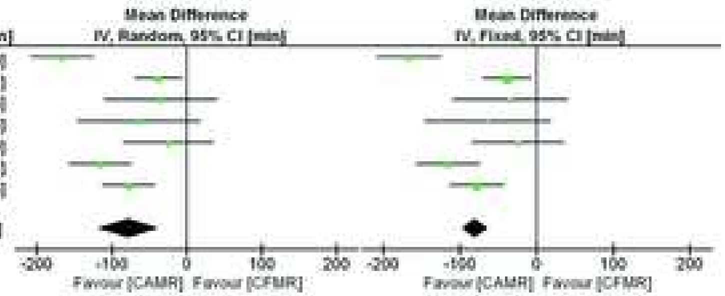
Study or Subgroup	CAMR Mean	CAMR SD	CAMR Total	CFMR Mean	CFMR SD	CFMR Total	Weight	Std. Mean Difference IV, Random, 95% CI	Weight	Std. Mean Difference IV, Fixed, 95% CI
Gil et al.	135	37	10	176	58	10	35.1%	-0.81 [-1.73, 0.11]	54.5%	-0.81 [-1.73, 0.11]
Zweifel et al	20.8	5.7	9	88.2	14.9	11	30.4%	-5.50 [-7.60, -3.40]	10.5%	-5.50 [-7.60, -3.40]
Tarsitano et al.	30.7	6.1	20	63.8	9.1	20	34.4%	-4.19 [-5.34, -3.04]	35.0%	-4.19 [-5.34, -3.04]
Total (95% CI)			39			41	100.0%	-3.40 [-6.23, -0.56]	100.0%	-2.48 [-3.16, -1.80]

Heterogeneity: Tau² = 5.73; Chi² = 29.17, df = 2 (P < 0.00001); I² = 93%
Test for overall effect: Z = 2.35 (P = 0.02) Random effect
Test for overall effect: Z = 7.16 (P < 0.00001) Fixed effect



Study or Subgroup	CAMR Mean [min]	CAMR SD [min]	CAMR Total	CFMR Mean [min]	CFMR SD [min]	CFMR Total	Weight	Mean Difference IV, Random, 95% CI [min]	Total	Weight	Mean Difference IV, Fixed, 95% CI [min]
Bao et al.	453.89	37.56	26	620.56	59.83	9	15.6%	-166.67 [-208.34, -125.00]	9	15.9%	-166.67 [-208.34, -125.00]
Bouchet et al	512.75	17.3	12	550.84	54.66	13	16.9%	-38.09 [-69.37, -6.81]	13	28.1%	-38.09 [-69.37, -6.81]
Culie et al.	481	95	18	516	102	11	11.4%	-35.00 [-109.56, 39.56]	11	5.0%	-35.00 [-109.56, 39.56]
Gil et al.	357	95	10	421	91	10	10.6%	-64.00 [-145.54, 17.54]	10	4.1%	-64.00 [-145.54, 17.54]
Ritschl et al.	526.63	75.42	16	551.29	89.64	14	13.3%	-24.66 [-84.41, 35.09]	14	7.7%	-24.66 [-84.41, 35.09]
Tarsitano et al.	435	62.7	20	550.5	69.7	20	15.7%	-115.50 [-156.59, -74.41]	20	16.3%	-115.50 [-156.59, -74.41]
Wang et al.	270	54	21	348	78	35	16.5%	-78.00 [-112.66, -43.34]	35	22.9%	-78.00 [-112.66, -43.34]
Total (95% CI)			123			112	100.0%	-77.54 [-117.77, -37.32]	112	100.0%	-80.13 [-96.72, -63.53]

Heterogeneity: Tau² = 2241.93; Chi² = 31.24, df = 6 (P < 0.0001); I² = 81%
Test for overall effect: Z = 3.78 (P = 0.0002) Random effect
Test for overall effect: Z = 9.47 (P < 0.00001) Fixed effect



Study or Subgroup	CAMR Mean [day]	CAMR SD [day]	CAMR Total	CFMR Mean [day]	CFMR SD [day]	CFMR Total	Weight	Mean Difference IV, Random, 95% CI [day]	Weight	Mean Difference IV, Fixed, 95% CI [day]
Bouchet et al	16.91	4.6	12	22.92	10.16	13	10.0%	-6.01 [-12.12, 0.10]	8.4%	-6.01 [-12.12, 0.10]
Culie et al.	29	10	18	29	11	11	6.0%	0.00 [-7.97, 7.97]	4.9%	0.00 [-7.97, 7.97]
Gil et al.	18	8	10	16	6	10	9.7%	2.00 [-4.20, 8.20]	8.2%	2.00 [-4.20, 8.20]
Ritschl et al.	16.94	5.72	16	20.93	11.53	14	8.5%	-3.99 [-10.65, 2.67]	7.1%	-3.99 [-10.65, 2.67]
Tarsitano et al.	13.8	2.8	20	17	4.9	20	44.1%	-3.20 [-5.67, -0.73]	51.3%	-3.20 [-5.67, -0.73]
Weitz et al.	18	8	24	18	6	26	21.7%	0.00 [-3.94, 3.94]	20.2%	0.00 [-3.94, 3.94]
Total (95% CI)			100			94	100.0%	-2.16 [-4.16, -0.15]	100.0%	-2.27 [-4.04, -0.49]

Heterogeneity: Tau² = 0.78; Chi² = 5.65, df = 5 (P = 0.34); I² = 11%
Test for overall effect: Z = 2.11 (P = 0.04) Random effect
Test for overall effect: Z = 2.51 (P = 0.01) Fixed effect

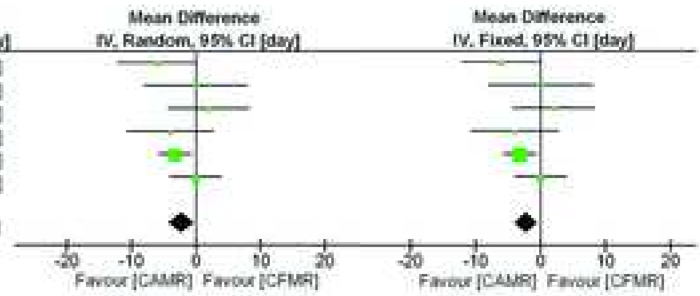


Figure 3

Study or Subgroup	CAMR Events	CAMR Total	CFMR Events	CFMR Total	Weight	Odds Ratio M-H, Random, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Gil et al.	0	10	2	10	17.5%	0.16 [0.01, 3.85]	32.7%	0.16 [0.01, 3.85]
Weitz et al.	2	24	2	26	42.1%	1.09 [0.14, 8.42]	24.1%	1.09 [0.14, 8.42]
Culie et al.	1	21	1	35	22.0%	1.70 [0.10, 28.70]	9.8%	1.70 [0.10, 28.70]
Tarsitano et al.	0	20	2	20	18.3%	0.18 [0.01, 4.01]	33.4%	0.18 [0.01, 4.01]
Total (95% CI)		**75**		**91**	**100.0%**	**0.62 [0.16, 2.33]**	**100.0%**	**0.54 [0.16, 1.85]**
Total events	3		7					

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.12$, df = 3 (P = 0.55); $I^2 = 0\%$

Test for overall effect: Z = 0.71 (P = 0.48) Random effect

Test for overall effect: Z = 0.98 (P = 0.33) Fixed effect