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Review

Benefits of 3D printing applications in jaw reconstruction: A systematic review and meta-analysis

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ABSTRACT

Background: Three-dimensional (3D) printing has changed surgical practice over the past few years, especially in maxillofacial surgery. However, little is known about its real clinical impact. The objectives of our study were to identify clinical outcomes that have been evaluated in the literature regarding 3D printing applications in jaw reconstruction, and to quantify the impact of this technology on operating times.
Methods: A systematic review was conducted by searching PubMed and EMBASE to collect comparative studies on 3D printing applications in jaw reconstruction. A meta-analysis of operating times was then performed. A Cochran's Q test was used to determine heterogeneity, and the overall effect size was calculated using a random effects model.
Results: Fourteen studies were included in our review. Eighteen clinical end-points were identified, of which the most frequently reported were operating time ($n = 5$; 35.7%) and the final aesthetic result ($n = 4$; 28.6%). Operating times were significantly lower in the 3D printing groups, with an overall estimated effect of 21.2% (95% CI 10–33%; $p < 0.001$).
Conclusion: The use of 3D printing in jaw reconstruction was associated with a significant reduction in operating times. The end-points evaluated differed largely among the studies. More studies with higher levels of evidence are needed to confirm our results.

1. Introduction

Three-dimensional (3D) printing is a major innovation that has changed surgical practice over the past few years. This technology allows the production of patient-specific anatomical models, surgical guides, and implants, thus introducing personalization to surgical practice (Rengier et al., 2010). Using CT or MRI images, prototypes of 3D objects are created by computer-aided design/computer aided manufacturing (CAD/CAM) technologies, and the final product is generated by adding materials layer by layer.

This technology is now well integrated into surgical practice, and almost all surgical subspecialties have embraced its use, including craniomaxillofacial surgery, orthopedic surgery, cardiovascular surgery, neurosurgery, plastic and reconstructive surgery, and liver surgery (Bartel et al., 2017; Hsieh et al., 2017; Jacobs and Lin, 2017; Louvrier et al., 2017; Pucci et al., 2017; Witowski et al., 2017). Most of the applications reported are for maxillofacial and orthopedic surgeries, including: 3D printing of anatomical models for preoperative planning and simulation, and the pre-bending of osteosynthesis plates; surgical guides for osteotomies, bone harvesting or screw placement; and personalized implants that accurately fit patient anatomy.

In maxillofacial surgery, 3D printing is mainly used in dental implant surgery and mandibular reconstruction (Louvrier et al., 2017). It is now a widely recognized surgical tool thanks to its numerous advantages reported in the literature, such as the accuracy of the medical devices produced, the ability to prepare implants prior to the operation, and reduced operating times (Martelli et al., 2016). When used in jaw reconstruction, it seems that this technology can improve both aesthetic outcome and functional

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rehabilitation (Wilde et al., 2014). However, despite a large number of studies in the literature reporting the use of 3D printing in jaw reconstruction, little is known about its real clinical benefits in comparison with conventional surgical techniques. Most of the data available are from case reports and case series, including only a small number of patients and without comparators.

The objective of our study was to evaluate the clinical impact of using 3D printing techniques in comparison with using conventional surgical techniques in jaw reconstruction. We performed a systematic review of comparative studies to identify the end-points evaluated, and the main outcomes observed.

2. Materials and methods

2.1. Systematic review

A systematic review was performed by searching PubMed and EMBASE to collect comparative studies on 3D printing applications in maxillofacial surgery. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were adopted to report the systematic review. The PRISMA checklist is available as supporting information (S1 Checklist). The search terms used were “three-dimensional printing and patients”, “additive manufacturing and patients”, “computer aided design and prosthesis design and patients” and “rapid prototyping and patients”. Studies were eligible if they included both patients treated with a surgical technique using 3D-printed medical devices (P) and those treated with the conventional surgical technique without using a custom-made device (C) for jaw reconstruction (I), in a hospital setting (S). The 3D printed medical devices could be anatomical models, surgical guides, and/or implants. All additive manufacturing techniques, such as direct metal laser sintering and fused deposition modeling, were considered in our study. Only comparative reports in French, English, or Spanish published between 2006 and 2017 were considered. A study protocol (S2 Appendix) was established to summarize eligibility criteria and the search terms used. Titles and abstracts were screened independently by two authors (CS and NM) to exclude irrelevant or duplicate abstracts. Exclusion criteria were as follows: review articles, studies without a comparison of clinical criteria, studies presented at a conference, fundamental research studies, and those with no application in maxillofacial surgery. Then, a full-text review was performed. Exclusion criteria were the same as in the first step. When the full-text of the publication was not available online, the article was directly requested from the corresponding author.

For eligible articles, data were recorded on a Microsoft Office Excel® 2016 spreadsheet and included: first author and date of publication, study design and number of patients, application (e.g. anatomical 3D printed models, surgical guides, and templates), comparators, the clinical criteria that had been evaluated, and significant outcomes obtained. All primary and secondary end-points compared in the included studies were extracted for analysis.

2.2. Meta-analysis

A meta-analysis of operating times was performed following the PRISMA guidelines. Mean operating times and standard deviation were collected from prospective studies and were recorded on a Microsoft Office Excel® 2016 spreadsheet. When data were not available in the text, they were directly requested from the corresponding author. A Cochran's Q test was performed to determine heterogeneity, and a random effects model was used to calculate the overall effect size. The significance of the effect size was determined using a standard-normal Z-test. A funnel plot was produced to assess publication bias. For each study, the risk of bias was independently assessed by two reviewers using the Cochrane risk of bias assessment tool (Higgins et al., 2011).

3. Results

3.1. Study selection

After excluding duplicates, 2815 studies were identified of which 2741 were excluded based on the content of their titles and abstracts. Subsequently, 74 studies remained in the selection process to be read in full, following which a further 60 were then excluded. Thus, a total of 14 studies met the selection criteria and were suitable for complete analysis (Fig. 1).

3.2. Characteristics of the included studies

The characteristics of the 14 included studies are summarized in Table 1. Of the 14 studies, 10 were prospective, of which four were randomized, and four were retrospective. Three-dimensional printing was used to produce surgical guides and templates ($n = 9$), anatomical models ($n = 8$), and implants ($n = 6$). They were mainly produced by laser sintering ($n = 7$) and powder bed inkjet ($n = 3$) techniques. Three studies did not clearly define the additive manufacturing method. The 14 studies included 351 patients (158 in the 3D printing groups and 193 in the control groups). They were mainly mandibular cases ($n = 329$; 93.7%), and the most reported indication was the reconstruction of defects resulting from oncological surgery.

3.3. Comparison of end-points

The end-points evaluated in the literature to demonstrate the benefit of 3D printing in jaw reconstruction were grouped into 17 different items. Table 2 summarizes the end-points evaluated and the outcomes observed. The end-points selected were very heterogeneous; six of them were evaluated in only one study. The most reported end-points were operating time ($n = 5$; 35.7%), final aesthetic result ($n = 4$; 28.6%), and the accuracy of the harvested transplant ($n = 4$; 28.6%).

3.4. Impact of 3D printing applications on operating times

Only two out of five studies comparing operating times demonstrated a reduction in this time with the use of 3D printing technology. This reduction varied greatly among the studies. The largest reduction in operating time (32.7%) was observed in a study that reported the use of patient-specific implants in jaw reconstruction (Sumida et al., 2015). Three studies showed that although overall operating times did not differ significantly between the two groups, there was a significant difference in specific surgical times, such as reconstruction time (Ayoub et al., 2014; de Farias et al., 2014; Sieira Gil et al., 2015; Tarsitano et al., 2016a), ischemic time, and osteosynthesis time (Ayoub et al., 2014). Three out of four studies evaluating reconstruction time defined it as the time taken from the initial shaping of the transplant at the donor site to the final osteosynthesis of the transplant (Ayoub et al., 2014; Sieira Gil et al., 2015; Tarsitano et al., 2016a). The remaining study restricted it to include only the time taken for osteosynthesis and flap molding at the defect site (de Farias et al., 2014).

Of the five prospective studies comparing operating times with and without the use of 3D printing, only four reported their mean operating time with standard deviation and only these studies were included in our meta-analysis (Fig. 2). These four studies

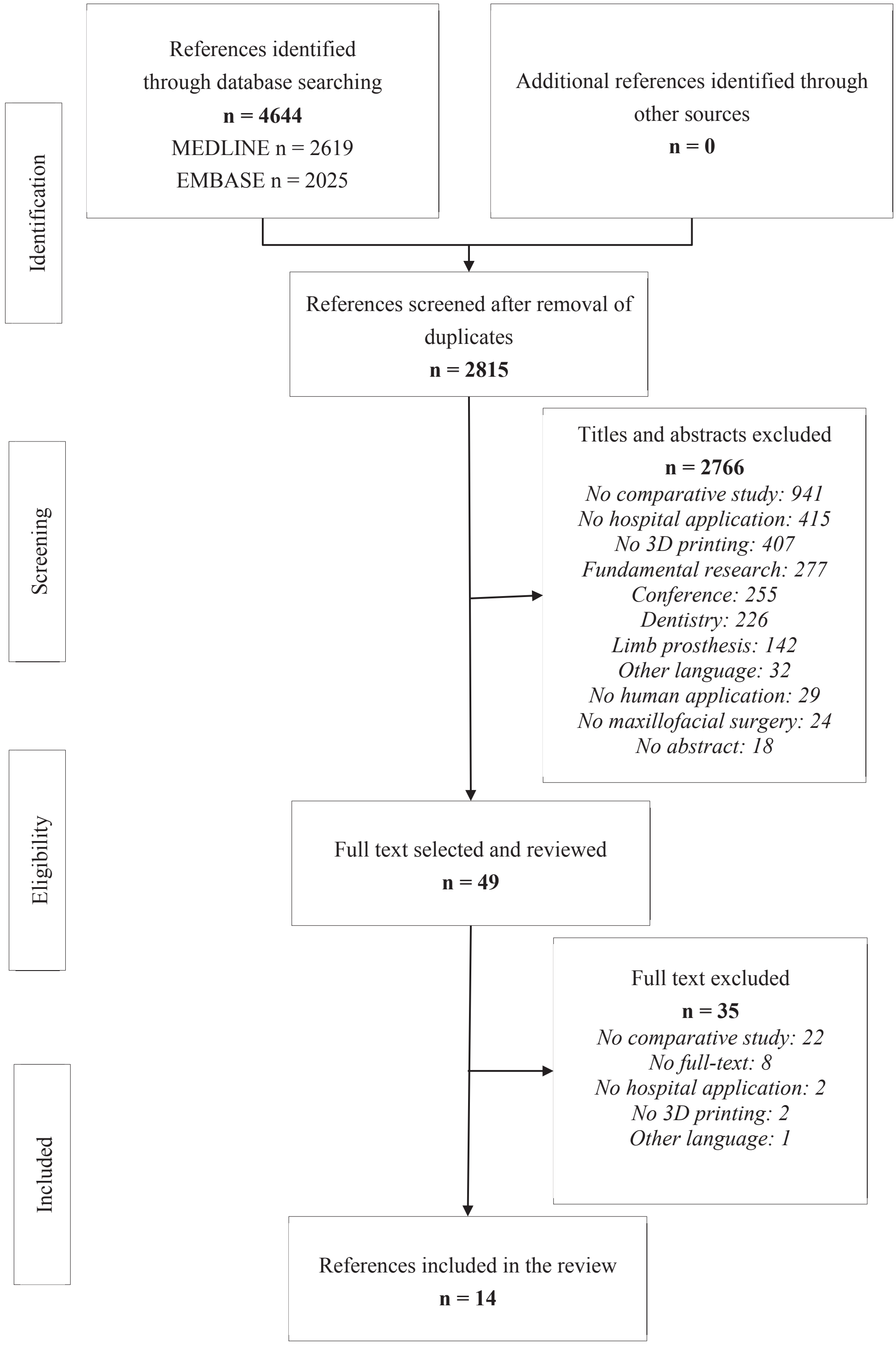

Fig. 1. PRISMA diagram.

included 106 patients (53 in the 3D printing groups and 53 in the control groups).

The funnel plot highlighted an important publication bias (Fig. 3). Only positive results demonstrating a reduction in operating times were published. Table 3 shows the risk of bias assessment for each included study. In all studies, a high risk of bias was noted for performance evaluation and outcome assessment due to the use of non-blinding protocols. Heterogeneity was significant among these studies ($I^2 = 67\%$, $p = 0.03$), so a random effect model was used. The overall estimated effect was 21.2%, demonstrating that the use of 3D printing led to a significant reduction in operating times.

3.5. *Impact of 3D printing applications on the final aesthetic result*

Four studies evaluated the impact of the 3D printed device by comparing the final aesthetic results, and all found a significant difference between control and experimental groups. The follow-

Table 1
Characteristics of the included studies.

First author, date, *Country*	Title	Applications	Study design	N° of patients in 3D group *(mandibular/ maxillary cases)*	N° of patients in control group *(mandibular/ maxillary cases)*	End-points	Outcomes
Al-Ahmad et al. (2013), *Jordan*	Evaluation of an innovative computer-assisted sagittal split ramus osteotomy to reduce neurosensory alterations following orthognathic surgery: a pilot study	Surgical guides and templates	Randomized prospective study	8 *(8/0)*	8 *(8/0)*	Neurosensory disturbance	On the computer-assisted SSRO (sagittal split ramus osteotomy) sides, patients had lower postoperative abnormal thresholds for the Semmes–Weinstein monofilaments on lower lip and chin ($p < 0.05$ at 3 months) and for the two-point discrimination on lower lip ($p < 0.05$ at 1 week) and chin ($p < 0.05$ at 6 months), with fewer abnormal self-reported changes in lower lip sensation ($p < 0.05$ at 1 week) after surgery.
Ayoub et al., (2014), *Germany*	Evaluation of computer-assisted mandibular reconstruction with vascularized iliac crest bone graft compared to conventional surgery: a randomized prospective clinical trial	Anatomical 3D printed models; surgical guides and templates	Randomized prospective study	10 *(10/0)*	10 *(10/0)*	Accuracy of the harvested transplant	In the computer-assisted group, the amount of bone harvested equaled the defect size, whereas the transplant size in the conventional group exceeded the defect site by 16.8 ± 5.6 mm ($p < 0.001$) on average.
						Complications	No statistical difference in blood loss ($p = 0.791$).
						Intercondylar distance	The intercondylar distance was measured before and after surgery; it was less affected in the computer-assisted group compared with the conventional group ($p < 0.001$).
						Ischemic time	Computer-assisted surgery shortened ischemic time in transplant patients (96.1 ± 15.8 versus 122.9 ± 20.4 min; $p < 0.005$).
						Length of hospital stay	No statistical difference between the two groups (17.5 ± 7.4 in 3D group; 19.1 ± 9.7 in control group; $p = 0.683$).
						Length of ICU stay	No statistical difference between the two groups (2.0 ± 0.9 in 3D group; 2.1 ± 2.1 in control group; $p = 0.894$).
						Operating time	No statistical difference between the two groups (498.5 ± 83.4 versus 525.2 ± 100.9 min; $p = 0.527$).
						Osteosynthesis time	Osteosynthesis time was significantly shorter in the computer-assisted group (10.1 ± 5.4 versus 18.2 ± 5.6 min; $p < 0.005$).

						Reconstruction time	Computer-assisted surgery shortened reconstruction time (16.4 ± 6.7 versus 38.5 ± 10.0 min; $p < 0.001$).
						Time to harvest	The time taken to saw and shape the transplant at the donor site was shorter using conventional surgery ($p < 0.005$).
Azuma et al., (2014), *Japan*	Mandibular reconstruction using plates prebent to fit rapid prototyping 3-dimensional printing models ameliorates contour deformity	Anatomical 3D printed models	Retrospective study	12 *(12/0)*	16 *(16/0)*	Final aesthetic result	The differential mandibular area and angle of the MRP group were significantly smaller than those of the conventional group ($p < 0.05$).
Ciocca et al., (2015), *Italy*	Accuracy of fibular sectioning and insertion into a rapid-prototyped bone plate, for mandibular reconstruction using CAD-CAM technology	Surgical guides and templates; implants	Retrospective study	5 *(5/0)*	5 *(5/0)*	Measurement of axes and angles	No statistically significant difference was observed between the test and control groups, neither between lateral and vertical shift or mesial and distal sections.
						Position of the fibular units	A difference, even though not significant, in the lateral shift of the mesial and distal positions of the fibular units was evident between groups.
Jiang et al., (2015), *China*	Functional evaluation of a CAD/CAM prosthesis for immediate defect repair after total maxillectomy: a case series of 18 patients with maxillary sinus cancer	Implants	Retrospective study	5 *(0/5)*	13 *(0/13)*	Final aesthetic result	Facial depression, and eyeball prolapse results showed improvements with prosthesis use at 1, 3, and 6 months after surgery ($p < 0.05$).
						Neurosensory disturbance	Speech intelligibility showed improvements with prosthesis use at 1, 3, and 6 months after surgery ($p < 0.05$). Swallowing function improved from level V to level II–IV with prosthesis use at 1, 3, and 6 months.
Mazzoni et al., (2013), *Italy*	Prosthetically guided maxillofacial surgery: evaluation of the accuracy of a surgical guide and custom-made bone plate in oncology patients after mandibular reconstruction	Anatomical 3D printed models; surgical guides and templates; implants	Prospective study	7 *(7/0)*	5 *(5/0)*	Measurement of axes and angles	No statistically significant difference was observed between the two groups regarding midline deviation, mandibular angle shift (except for the left angle shift on the lateral plane) and condylar position. With regard to angular deviation of the body axis, the data showed a significant difference in the arch deviation.
Modabber et al., (2012), *Germany*	Computer-assisted mandibular reconstruction with vascularized iliac crest bone graft	Anatomical 3D printed models; surgical guides and templates	Retrospective study	5 *(5/0)*	15 *(15/0)*	Accuracy of the harvested transplant	In the 3D group, the graft fitted perfectly into the mandibular defect without major adjustments for all patients. In the conventional surgery group, the harvested amount of bone exceeded the required amount

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Table 1 (*continued*)

First author, date, *Country*	Title	Applications	Study design	N° of patients in 3D group *(mandibular/maxillary cases)*	N° of patients in control group *(mandibular/maxillary cases)*	End-points	Outcomes
							by an average of 25.3 mm (range = 13.1–33.6 mm).
						Ischemic time	The average ischemic time decreased by 15.6 min (range = 7.3–22.8 min) compared with that of conventional surgery.
Modabber et al., (2012), *Germany*	Evaluation of computer-assisted jaw reconstruction with free vascularized fibular flap compared with conventional surgery: a clinical pilot study	Anatomical 3D printed models; surgical guides and templates	Randomized prospective study	5 *(2/3)*	5 *(4/1)*	Accuracy of the harvested transplant	In the 3D group, there was no change between the defect size of the fibula and the necessary transplant size. In conventional surgery, a mean change of 1.92 cm occurred ($p = 0.001$).
						Ischemic time	Ischemic time was significantly shorter in the 3D group versus conventional surgery ($p = 0.014$).
						Time to harvest	Shaping procedure was significantly shorter in the 3D group versus conventional surgery ($p = 0.014$).
de Farias et al. (2014), *Brazil*	Use of prototyping in preoperative planning for patients with head and neck tumors	Anatomical 3D printed models	Randomized prospective study	17 *(17/0)*	20 *(20/0)*	Accuracy of the harvested transplant	Results showed a tendency to reduce the size of the bone flap taken for reconstruction with a remaining bone flap of 2.1 cm in the 3D group, ranging from 0 to 6 cm, and 8.7 cm in the control group, ranging from 5.5 to 13 cm.
						Final aesthetic result	Better aesthetic results were obtained in the 3D group than in the conventional surgery group.
						Osteosynthesis time	The osteosynthesis time was 30.42 min in the 3D group versus 86.66 min in the control group ($p = 0.001$).
						Reconstruction time	Reconstruction time was significantly shorter in the 3D group (43.70 min versus 127.77 min in group B; $p = 0.001$).
						Screw insertion time	No statistical difference was observed in the duration of screw insertion (20 min in the 3D group versus 38.11 min in the control group).
						Time to harvest	No significant difference was observed (108.50 min in the 3D group and 141.10 min in the control group).

Sieira Gil et al., (2015), *Spain*	Surgical planning and microvascular reconstruction of the mandible with a fibular flap using computer-aided design, rapid prototype modeling, and precontoured titanium reconstruction plates: a prospective study	Anatomical 3D printed models; surgical guides and templates	Prospective study	10 *(10/0)*	10 *(10/0)*	Complications	Significant differences in the incidence of dental malocclusion ($p = 0.03$) and exposure of the titanium plate ($p = 0.009$) were observed, with higher incidences in the control group.
						Length of hospital stay	No significant difference was observed (18 days in the 3D group and 16 days in the control group; $p = 0.58$).
						Operating time	No significant difference in the operating time was found (357 min in the 3D group versus 421 min in the control group; $p = 0.14$).
						Reconstruction time	The mean operating time for reconstruction in the preoperative planning group was 135 min compared with 176 min in the conventional group ($p = 0.04$).
Sumida et al., (2015), *Japan*	Custom-made titanium devices as membranes for bone augmentation in implant treatment: clinical application and the comparison with conventional titanium mesh	Implants	Prospective study	13 *(13/0)*	13 *(13/0)*	Complications	No significant difference in the incidences of complications was observed ($p = 0.27$).
						Number of trays/ screws used	The number of screws used was significantly fewer in the custom-made group than in the control group ($p < 0.01$).
						Operating time	The operation time of the custom-made group (75.4 ± 11.6 min) was significantly shorter than that of the conventional group (111.9 ± 17.8 min) ($p < 0.01$).
Tarsitano et al., 2016, *Italy*	Is a computer-assisted design and computer-assisted manufacturing method for mandibular reconstruction economically viable?	Surgical guides and templates; implants	Prospective study	20 *(20/0)*	20 *(20/0)*	Cost	The money saved as a result of the time gained in the operating room was €3450. This cost corresponds approximately to the total price of the CAD-CAM surgery.
						Length of hospital stay	The mean overall lengths of hospital stay were 13.8 days for the CAD-CAM group and 17 days for the freehand group.
						Operating time	The mean operating time for the CAD-CAM group was 435 min, whereas that for the freehand group it was 550.5 min.
						Reconstruction time	The mean reconstructive time was 30.7 (range, 21–41) minutes for the 3D group and 63.8 (range, 45–79) minutes for the control group ($p = 0.041$).

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Table 1 (*continued*)

First author, date, *Country*	Title	Applications	Study design	N° of patients in 3D group (*mandibular/maxillary cases*)	N° of patients in control group (*mandibular/maxillary cases*)	End-points	Outcomes
Tarsitano et al., 2016, *Italy*	Morphological results of customized microvascular mandibular reconstruction: a comparative study	Surgical guides and templates; implants	Prospective study	30 *(30/0)*	30 *(30/0)*	Final aesthetic result	The mean differences registered between preoperative and postoperative CT scans were significantly better for the test group regarding chin protrusion ($p = 0.05$).
						Measurement of axes and angles	The mean differences registered between preoperative and postoperative CT scans were significantly better for the test group regarding mandibular angle ($p = 0.034$) and bigonial diameter ($p = 0.041$). No significant differences were registered for midline deviation ($p = 0.092$).
Zhang et al., (2011), *China*	Application of rapid prototyping for temporomandibular joint reconstruction	Anatomical 3D printed models	Prospective study	11 *(11/0)*	11 *(11/0)*	Operating time	The operative time was significantly longer in the control group than that in the 3D group (7.09 h versus 5.67 h, respectively; $p < 0.05$).

up duration varied from 1 month to 1 year. Three out of the four studies used objective criteria based on image analysis to assess the aesthetic outcome (Azuma et al., 2014; Jiang et al., 2015; Tarsitano et al., 2016b). For the remaining study, the analysis was based on subjective evaluation of postoperative photographs by blinded medical and non-medical individuals.

3.6. *Impact of 3D printing applications on the accuracy of the harvested transplant*

Of the four studies evaluating the accuracy of the harvested transplant, three of them compared the difference between the size of the bone flap removed and the size of the bone flap required (Modabber et al., 2012a, 2012b; Ayoub et al., 2014). Two out of these three studies demonstrated a significant reduction in this difference for the 3D printing group (Modabber et al., 2012b; Ayoub et al., 2014).

In the remaining study, this end-point was evaluated by measuring the size of the bone flap taken. The authors showed that this tended to be smaller when 3D printed surgical guides were used (de Farias et al., 2014).

3.7. *Impact of 3D printing applications on the incidence of complications*

Three studies compared complications between control and experimental groups. Sieira Gil et al. reported 11 different complications, such as hematoma or infection, and found a statistical difference for only two of them (dental malocclusion and exposure of the titanium plate) (Sieira Gil et al., 2015). Blood loss was evaluated in one study by analyzing the number of applied units of erythrocytes and no statistical difference was found (Ayoub et al., 2014). This study also demonstrated that the transplant survival rate was identical between the two groups (90%). The remaining study compared the infection rates (23.1% versus 7.7%) and incidence of mucosal rupture (23.1% versus 7.7%) between the conventional surgery group and the experimental group, respectively, and no statistically significant difference was found ($p = 0.27$) (Sumida et al., 2015).

3.8. *Impact of 3D printing applications on the length of hospital stay*

Three studies compared the length of hospital stay, which varied from 13.8 days to 17.5 days in the experimental groups and from 16 days to 19 days in the control groups (Ayoub et al., 2014; Sieira Gil et al., 2015; Tarsitano et al., 2016a). One study found that the length of stay was higher in the experimental group than in the control group (Sieira Gil et al., 2015). However, none of the studies found a statistically significant difference.

4. Discussion

To our knowledge this is the first systematic review aiming to evaluate the clinical impact of 3D printing in jaw surgery. In the past decade, many studies have underlined the advantages that 3D printing could bring to surgery, such as the possibility of preoperative planning, which could improve the self-confidence of the surgeon, or the use of specific instruments or implants that accurately fit the patient's anatomy. Nevertheless, these studies were mainly case reports or case series involving fewer than 10 patients (Louvrier et al., 2017). Although low-cost 3D printers are available, additional costs associated with this technology remain a major limiting factor to its widespread use. To analyze cost effectiveness,

Table 2
End-points evaluated in the included studies and the outcomes observed.

End-points	Number of studies	Statistical difference in favor of 3D printing	No statistical difference between the two groups
Operating time	5	Zhang et al. (2011) Sumida et al. (2015)	Ayoub et al. (2014) Sieira Gil et al. (2015) Tarsitano et al. (2016a)
Final aesthetic result	4	de Farias et al. (2014) Azuma et al. (2014) Jiang et al., (2015) Tarsitano et al., (2016b)	
Accuracy of the harvested transplant	4	Modabber et al. (2012b) Ayoub et al. (2014)	de Farias et al. (2014) Modabber et al. (2012a)
Reconstruction time	4	Ayoub et al., (2014) de Farias et al. (2014) Sieira Gil et al. (2015) Tarsitano et al. (2016a)	
Complications	3	Sieira Gil et al. (2015)[a]	Ayoub et al. (2014) Sumida et al. (2015) Sieira Gil et al. (2015)[a]
Ischemic time	3	Modabber et al. (2012a) Modabber et al. (2012b) Ayoub et al. (2014)	
Length of hospital stay	3		Ayoub et al. (2014) Sieira Gil et al., (2015), Tarsitano et al. (2016a)
Measurement of axes and angles	3	Mazzoni et al. (2013)[a] Tarsitano et al. (2016b)	Mazzoni et al. (2013)[a] Ciocca et al. (2015) Tarsitano et al. (2016b)
Time to harvest	3	Modabber et al., (2012b) de Farias et al. (2014)	Ayoub et al. (2014)
Neurosensory disturbance	2	Al-Ahmad et al., (2013) Jiang et al., (2015)	
Osteosynthesis time	2	de Farias et al. (2014) Ayoub et al. (2014)	
Cost	1		Tarsitano et al. (2016a)
Intercondylar distance	1	Ayoub et al. (2014)	
Length of stay in ICU	1		Ayoub et al. (2014)
Number of trays/screws used	1	Sumida et al. (2015)	
Position of the fibular units	1		Ciocca et al. (2015)
Screw insertion time	1	de Farias et al. (2014)	

[a] Some studies are indicated in both right-hand columns for some end-points because the results were significantly different for only some of the end-points evaluated.

Author	Control group: Operating time (mins)	Control group: N° of patients	3D printing group: Operating time (mins)	3D printing group: N° of patients	Weight	Random effect model: Reduction in operating time	Random effect model: Confidence Interval (95%)
AYOUB *et al.*[11]	525.2 100.9	10	498.5 83.4	10	21%	5.1%	-10.3% - 20.5%
SIEIRA *et al.*[12]	176 58.0	10	135 37.0	10	12%	23.3%	-0.9% - 47.5%
SUMIDA *et al.*[10]	111.9 18.5	13	75.38 11.6	13	29%	32.6%	22.0% - 43.2%
TARSITANO *et al.*[13]	550.5	20	435 27.0	20	38%	21.0%	16.2% - 25.8%
		53		**53**	100%	**21.2%**	**10.0% - 33.0%**

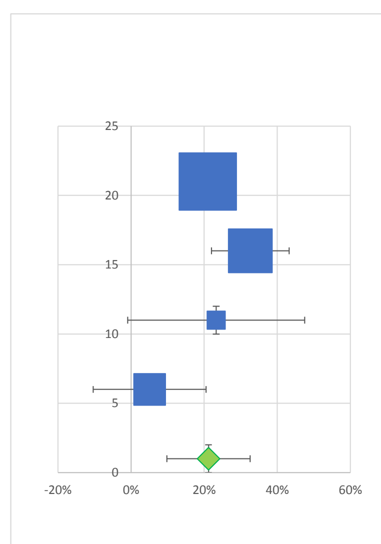

Fig. 2. Mean operating times for control group versus 3D printing group: Q = 9.0; DoF = 3; I^2 = 67%; p = 0.03; Z = 0.54.

it is important to objectively determine the impact of 3D printing on clinical outcomes.

Four out of the 14 included studies were prospective and randomized studies. Considering that 3D printing technology has only recently been adopted by surgeons, and in comparison with results obtained in a previous study we conducted (Martelli et al., 2016), this is more than expected. Up until the last few years, the use of 3D printing was limited to complex cases that could not be treated using conventional methods. Consequently, the literature was mainly composed of case reports, and data were abundant for this highly individualized use of 3D printing. Nowadays, 3D printing seems to be more accessible. Surgeons can now apply this technology to a larger number of patients, sometimes in their routine surgical practice. This allows prospective comparative studies to be performed that generate data with higher levels of evidence.

This systematic review shows that a wide range of end-points have been used to evaluate the effectiveness of 3D printing, and the reasons given as to why such end-points were selected are often

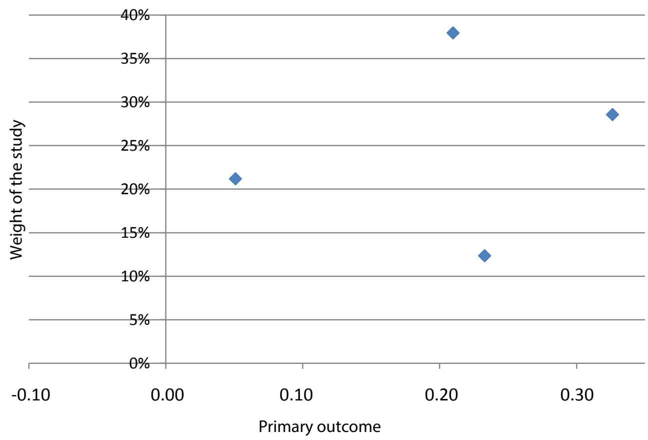

Fig. 3. Funnel plot evaluating the publication bias.

Table 3
Risk of bias assessment (Cochrane risk of bias assessment tool).

Study	A	B	C	D	E	F	G
Ayoub et al. (2014)	−	−	−	?	+	+	−
Sieira Gil et al. (2015)	+	+	−	?	+	+	−
Sumida et al. (2015)	+	?	−	?	+	+	−
Tarsitano et al. (2016a)	+	+	−	?	+	+	−

A: selection bias — random sequence generation; B: selection bias — allocation concealment; C: reporting bias — selective reporting; D: other sources of bias; E: performance bias — blinding (participants and personnel); F: detection bias — blinding (outcome assessment); G: incomplete outcome data.

not clearly explained. The end-points most commonly evaluated in the included studies were operating time and final aesthetic result. This was also observed in a systematic review reporting all the end-points used to evaluate the effectiveness of 3D printing in all surgical domains (Diment et al., 2017). It is comprehensible that operating time is often used to evaluate this technology, because it is an objective and easily reportable element with a direct impact on the incidence of complications and costs.

This meta-analysis of jaw reconstruction demonstrates that operating time is significantly reduced when a surgeon uses a 3D printed medical device. This reduction is linked, on the one hand, to a reduction in the time needed to harvest the bone flap (Modabber et al., 2012b; de Farias et al., 2014), and on the other hand, to the time needed to reconstruct the defect (Ayoub et al., 2014; de Farias et al., 2014; Sieira Gil et al., 2015; Tarsitano et al., 2016a). This is made possible by the opportunity for preoperative planning and the use of patient-specific instrumentation. It is worth noting that 3D printing has only ever been used to guide the osteosynthesis part of the intervention, but never the vascular part. Yet the vascular stage of the surgery is very complex, and the successful application of 3D printing techniques to this stage would directly impact flap survival and postoperative complications. Few studies have evaluated the duration of the vascular repair stage, so it would be very interesting to measure this in order to appreciate its impact on overall surgical time. This would help to determine how 3D printing applications can better assist maxillofacial surgeons.

The second end-point most evaluated in the included studies was the final aesthetic result, showing a tendency to achieve better aesthetic results with the use of 3D printing technology. In jaw reconstruction it is important to obtain good aesthetic results because this directly impacts on functional rehabilitation, neurosensory disturbance, and thus quality of life. Nevertheless, an objective evaluation of this end-point is difficult, and we noted that in all the included studies little attention was given to patient satisfaction. In addition, patients were followed over a short period, so a long-term follow-up of these patients will be essential to confirm these results.

This systematic review also observed a lack of homogeneity in how techniques have been reported in material and methods sections. Indeed, the 3D printing techniques and materials used are rarely described, although they affect the quality of the 3D-printed device and thus its effectiveness. In the future, it will be necessary to identify which technique offers the best value for money for each type of surgery and application. Also, the end-points evaluated in these studies were very heterogeneous and not always clearly defined. This issue made the comparison of results among studies difficult.

The quality assessment of the included studies in the meta-analysis showed a risk of bias for the outcome evaluation due to the assessor's knowledge of the allocated intervention. This is a recurring issue for the clinical evaluation of medical devices. Blinding outcome assessors may be difficult when the intervention is evaluated during the procedure, such as for the measurement of operating time. However, blinding could be performed when the effectiveness is evaluated remotely, such as for the aesthetic result for example. In this case, it would be possible to achieve single blinding by the use of independent outcome assessors (Sedrakyan et al., 2010). Regarding the publication bias, it is not surprising that only positive results in favor of 3D printing technology were found in the literature. Negative results are often considered as an absence of results by the authors, and journals are more likely to publish positive results (Bown and Sutton, 2010).

Our study has some limitations that are worth mentioning. First, our systematic review only included articles published in English, French, or Spanish, and a search for non-published data was not conducted. This might also introduce a bias in the results. However, we considered that studies published in English were representative of the overall literature and that non-published data could be less robust than published data, thus introducing a quality bias. Finally, another limitation of our study is that although each full-text article was requested from the corresponding author, some articles could not be collected and were excluded from the complete analysis.

5. Conclusion

Our work shows that the use of 3D printing for jaw reconstruction is likely to be associated with a reduction in operating times and better aesthetic outcomes. However, to confirm our results, more studies with higher levels of evidence are needed. This will only be possible if guidelines are established for the clinical evaluation of 3D printing in surgery.

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Declarations of interest

None.

Contributors

CS and NM participated in the conception and design of the study, acquisition of data, and analysis and interpretation of data.

CS, HVDB, and NM participated in drafting the article or revising it critically for important intellectual content.

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Appendix A. Supplementary data

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