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REVIEW ARTICLE

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Static computer-aided, partially guided, and free-handed implant placement: A systematic review and meta-analysis of randomized controlled trials

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Abstract

Objective: To analyze the outcomes of static computer-aided implant placement (sCAIP) compared to partially guided (PGIP) and free-handed (FHIP) implant placement.

Material and Methods: This study was registered in PROSPERO (CRD42019131397). A comprehensive literature search was performed by two independent examiners. Only randomized controlled trials (RCTs) were selected. Treatment modalities included sCAIP, PGIP, and FHIP. Data pertaining to the outcomes of interest were extracted. Random-effects meta-analyses were feasible for a subset of outcomes.

Results: From an initial list of 2,870 records, fourteen articles for a total of ten RCTs were selected. Data from 7 of these studies allowed for the conduction of three meta-analyses comparing accuracy of implant placement across modalities. Survival rate up to 12 months post-loading was high (>98%) and comparable between treatments (low-quality evidence). No tangible differences in terms of patient perception of intra- or postoperative discomfort were observed (low-quality evidence). Quantitative analyses revealed significantly lower angular (MD = 4.41°, 95% CI 3.99–4.83, $p < .00001$), coronal (MD = 0.65 mm, 95% CI 0.50–0.79, $p < .00001$), and apical (MD = 1.13 mm, 95% CI 0.92–1.34, $p < .00001$) deviation values for sCAIP as compared to FHIP (8 studies, 383 patients, 878 implants, high-quality evidence). A similar discrepancy, in favor of sCAIP, was observed for angular deviation only as compared to PGIP (MD = 2.11°, 95% CI 1.06–3.16, $p < .00001$).

Conclusions: sCAIP is associated with superior accuracy compared to PGIP and FHIP.

KEYWORDS

clinical assessment, clinical research, clinical trials, diagnosis, surgical techniques

1 | INTRODUCTION

Congruent with current global trends, a steady increase in implant therapy use is expected in developed countries until the year 2026 (Elani, Starr, Da Silva, & Gallucci, 2018). While implant therapy has been proven as a viable method for tooth replacement, a plethora of variables may play a significant role in its biological, functional, and esthetic outcomes. Some of these critical factors are related to

specific local and systemic characteristics of the host (Hammerle & Tarnow, 2018; Suarez-Lopez Del Amo, Lin, Monje, Galindo-Moreno, & Wang, 2016), final implant position (Canullo et al., 2016; Saleh et al., 2018), implant placement and/or loading technique (D'Haese, Ackhurst, Wismeijer, De Bruyn, & Tahmaseb, 2017; Morton & Pollini, 2017), and prosthetic design (Katafuchi, Weinstein, Leroux, Chen, & Daubert, 2018; Su, Gonzalez-Martin, Weisgold, & Lee, 2010).

Over the past several years, computer-aided implant placement (CAIP) protocols, which are based on digital workflows aimed at maximizing implant placement accuracy, have expanded the landscape of existing surgical options (Vandenberghe, 2018). CAIP can be categorized as either dynamic (dCAIP), which involves software-based intraoperative feedback mechanisms on handpiece position, or static (sCAIP), which is a more widely extended modality that precludes intraoperative modification of implant position due to the use of a restrictive surgical guide generated on the basis of preoperative digital planning (D'Haese et al., 2017; Jung et al., 2009). The fabrication of surgical guides employed in sCAIP is performed through a high-precision process known as three-dimensional (3D) additive manufacturing (Revilla-Leon, Sadeghpour, & Ozcan, 2019).

The body of evidence in this field has grown substantially over the past decade, including several systematic reviews aimed at evaluating the clinical effectiveness of sCAIP, particularly its accuracy, compared to other surgical modalities (Bover-Ramos, Vina-Almunia, Cervera-Ballester, Penarrocha-Diago, & Garcia-Mira, 2018; Pozzi, Polizzi, & Moy, 2016; Van Assche et al., 2012; Zhou, Liu, Song, Kuo, & Shafer, 2018). Nonetheless, the accuracy of implant placement only addresses one facet of sCAIP. Other relevant outcome measures are cost-effectiveness (Joda, Derksen, Wittneben, & Kuehl, 2018; Ravida et al., 2018; Younes, Eghbali, De Bruyckere, Cleymaet, & Cosyn, 2019), patient's perception of treatment, impact on quality of life, and postoperative morbidity, which are variables that may determine the choice of implant placement modality in numerous clinical situations.

It was therefore the aim of this systematic review to comprehensively analyze the clinical, digital, and patient-centered outcomes of sCAIP compared to other implant placement modalities.

2 | MATERIALS AND METHODS

The protocol of this review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the identification code CRD42019131397. The conduction of this review fully adhered to the guidelines of the Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, Altman, & Group, 2009).

2.1 | Definitions

Due to some degree of heterogeneity in the terminology used to define interventional methods and outcome measures within the literature, a set of definitions is provided in order to consolidate existing terminological variations for ease of data synthesis and comprehension. The definitions concerning treatment approach are as follows:

- **Free-handed implant placement (FHIP):** Conventional approach involving osteotomy preparation and implant placement via mental navigation and exclusive of any surgical guide that may direct or influence the course of placement into the recipient site.
- **Partially guided implant placement (PGIP):** Approach of osteotomy preparation and implant placement by way of employing a prosthetically driven surgical guide, with some to no consideration of the underlying bone morphology. Guide fabrication may be based on a preoperative dental stone cast of the recipient arch or 3D-printed. Depending on its design, the guide may be employed solely for the initial osteotomy or for partial or complete osteotomy expansion, typically in a non-restrictive manner. In this modality, upon completion of the osteotomy, implant placement is done free-handed, with no direct surgical guide support.
- **Computer-aided implant placement (CAIP)**

  a. Dynamic (dCAIP): Fully guided approach of osteotomy preparation and implant placement via the application of "a surgical navigation system that reproduces the virtual implant position directly from computerized tomographic data and allows intra-operative changes of the implant position" (D'Haese et al., 2017).
  b. Static (sCAIP): Fully guided approach involving restrictive osteotomy preparation and implant placement through a prosthetically driven surgical guide fabricated on the basis of preoperative computerized tomographic and stereolithographic data.

The definitions concerning accuracy outcome measures are as follows:

- **Depth Deviation:** Metric discrepancy (measured in millimeters) between the planned and actual implant position in the vertical plane relative to the long axis of the implant body; primarily ascribed to the varying number of turns during final placement (Figure 1a).
- **Angular Deviation:** Angular discrepancy (measured in degrees) between the planned and actual implant position respective to the center of the implant body; primarily ascribed to the variation in point of entry (Figure 1b).
- **3D Bodily Deviation:** Metric discrepancy (measured in millimeters) between the planned and actual implant position in the bucco-lingual and/or mesio-distal planes relative to the coronal- and apical-most regions of the implant body; ascribed to a combination of preoperative and intraoperative factors (Figure 1c).

2.2 | Clinical scenarios of interest

Edentulous sites, either maxillary or mandibular, anterior or posterior, single- or multi-tooth, in which placement of dental implants via

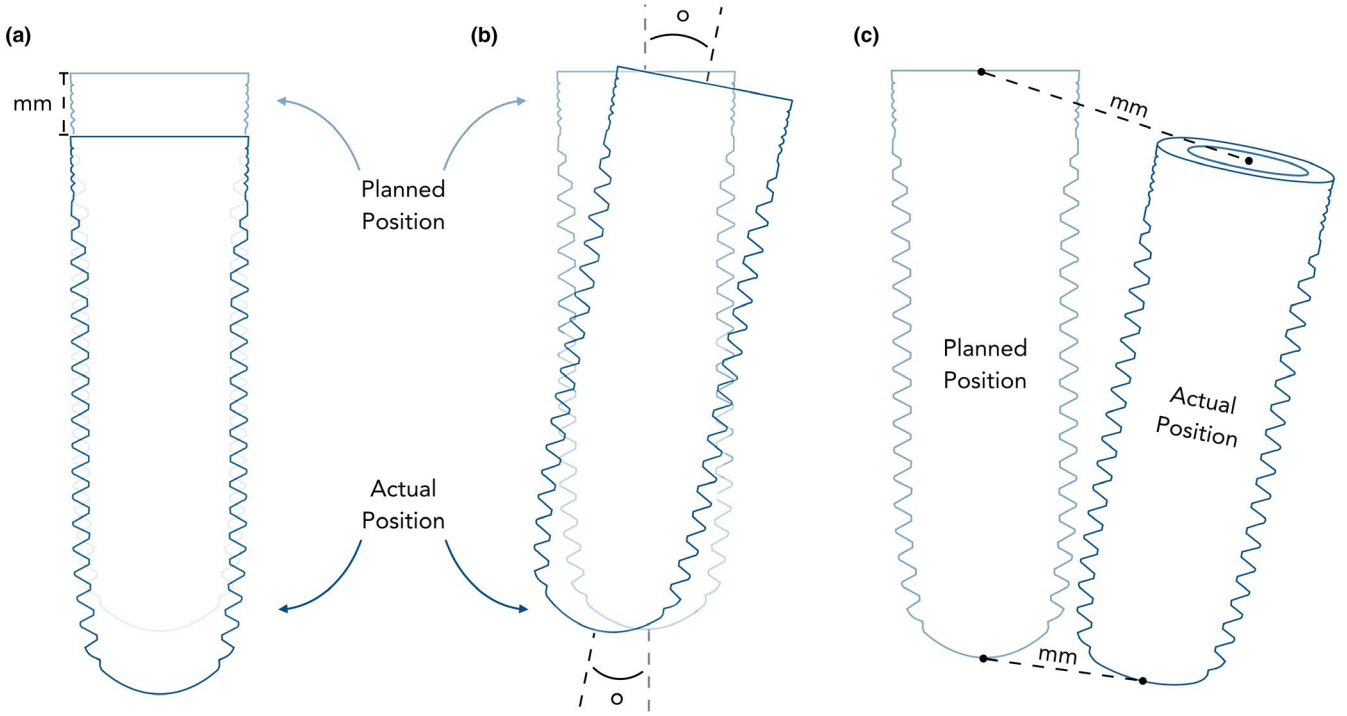

FIGURE 1 Illustrations depicting (a) depth, (b) angular, and (c) 3D bodily implant deviation

sCAIP (test) or through a conventional approach (FHIP or PGIP) not involving sCAIP (control) was indicated.

2.3 | PICO question

The central clinical question of this systematic review was formatted according to the PICO (Population, Intervention, Comparison and Outcomes) framework for evidence-based practice (Stone, 2002):

"What are the clinical, digital and patient-reported outcome measures (PROMs) associated with static computer-aided compared to conventionally placed dental implants (free-handed or partially guided) in adult human subjects?"

- Population: Adult human subjects in need of one or more dental implants for tooth replacement.
- Intervention: Static computer-aided placement of one or more dental implant followed by functional loading ≥3 months later.
- Comparison: Conventional (FHIP or PGIP) placement of one or more dental implants followed by functional loading ≥3 months later.
- Outcomes of interest:
  1. Clinical: Implant survival and implant success on the basis of the criteria reported in the selected studies.
  2. Digital (Radiographic and/or Stereolithographic): Marginal bone level and accuracy of implant placement or deviation from planned implant placement (in degrees and/or mm).
  3. PROMs: Postoperative morbidity, patient satisfaction, and changes in quality of life subsequent to implant placement.

2.4 | Eligibility criteria

An article was deemed eligible if it reported a randomized controlled clinical trial that enrolled adult human subjects older than 18 years of age who had at least one implant and one abutment placed in one of the aforementioned clinical scenarios of interest. Studies must have compared sCAIP (test) to either partially guided or free-handed protocols that do not involve the use of a restrictive surgical guide for implant placement (control). Non-controlled prospective, cohort, cross-sectional, ex vivo, and in vitro studies, as well as reviews and editorials, were considered non-eligible. Studies that enrolled uncontrolled diabetics, heavy smokers (>10 cigs/day), or subjects that suffered from any local or systemic condition known to considerably affect osseointegration were excluded. No (upper limit) age or sex restriction was set. No minimum number of patients per group was set. For inclusion, a study must have reported at least one of the outcomes of interest captured in the PICO question. For study series that used the same population, only the study with the longest follow-up was included in both the qualitative and quantitative analyses.

2.5 | Types of outcome measures

Accuracy of placement, defined as (angular, coronal and apical) deviation between planned and actual implant position, was defined by mean differences in the data analyses.

2.6 | Information sources and literature search protocol

Three electronic databases were utilized to identify articles that satisfied the eligibility criteria, namely National Library of Medicine (MEDLINE–PubMed), Cochrane Central Register of Controlled Trials (CENTRAL) and EMBASE. The last search was conducted on March 1st, 2020. The following combination of text keywords and indexed (MeSH) terms connected by Boolean operators was used to create a comprehensive query: "implant", "dental implant", "osseointegration", " implant placement", "free-handed implant placement", "bone remodeling", "bone resorption", "bone loss", "bone defect", "implant failure", "dental implant success", "computer guided implant placement", "implant accuracy", "surgery", "computer-assisted", "surgery", "computer-aided", "image-guided surgery." No search restriction was set regarding language of the article, publication date, or publication status. As an example, the full search strategy for one of the databases of interest is displayed in Table 1.

In order to complement the database search, a manual search through relevant scientific journals (*Clinical Oral Implants Research*, *International Journal of Oral and Maxillofacial Implants*, *Journal of Implant Dentistry and Related Research*, *International Journal of Oral Implantology*, *European Journal of Oral Implantology*, *Implant Dentistry*, *Journal of Oral Implantology*, *Journal of Clinical Periodontology*, *Journal of Periodontology*, *International Journal of Periodontics and Restorative Dentistry*, *Journal of Oral and Maxillofacial Surgery*) was conducted in order to identify any other publications and ensure a thorough screening process. Additionally, cross-referencing of cited references in 22 systematic reviews on the topic (Bover-Ramos et al., 2018; Carbajal Mejia, Wakabayashi, Nakano, & Yatani, 2016; Colombo et al., 2017; D'Haese et al., 2012; D'Haese, Van De Velde, Komiyama, Hultin, & De Bruyn, 2017; Hultin, Svensson, & Trulsson, 2012; Joda et al., 2018; Jung et al., 2009; Laederach, Mukaddam, Payer, Filippi, & Kuhl, 2017; Laleman et al., 2016; Moraschini, Velloso, Luz, & Barboza, 2015; Pozzi et al., 2016; Raico Gallardo et al., 2017; Schneider, Marquardt, Zwahlen, & Jung, 2009; Schnitman, Hayashi, & Han, 2014; Seo & Juodzbalys, 2018; Sigcho Lopez, Garcia, Da Silva Salomao, & Cruz Lagana, 2019; Van Assche et al., 2012; Vercruyssen, Hultin, et al., 2014; Voulgarakis, Strub, & Att, 2014; Widmann & Bale, 2006; Zhou et al., 2018) was conducted for additional article identification.

TABLE 1 Search strategy used for one of the databases of interest in the article identification phase

PubMed via MEDLINE Search Strategy
#1 implant OR dental implant OR implant* OR osseointegration OR implant placement OR free-handed implant placement
#2 bone remodeling OR bone resorption OR bone loss OR bone defect OR implant failure OR dental implant success
#3 #1 OR #2
#4 computer guided implant placement AND implant accuracy
#5 surgery, computer-assisted OR surgery, computer-aided OR image-guided surgery OR surgery, image-guided OR therapy, computer-assisted AND dental
#6 #4 OR #5
#7 #3 AND #6

2.7 | Article selection

Two reviewers (M.T. and G.A.) independently read the title and abstract of the entries obtained from the literature searches. Both reviewers then individually read through the full-text versions of the studies that would be potentially eligible. Final article selection for qualitative and/or quantitative analysis, on the basis of the aforementioned eligibility criteria, was performed thereafter. When disagreement in the final selection of a study arose, resolution was first endeavored through open discussion between the two reviewers. In the case that no agreement could be achieved, the two reviewers sought arbitration from another co-author (L.C.).

2.8 | Data extraction

The data extraction process was executed by one of the authors (M.T.). The collected data were verified independently by the remaining authors (L.C. and G.A.) in order to ensure accuracy as free from human error as possible. In addition to the outcomes of interest of this review, ancillary study information collated in the data collection forms included the following: first author, country in which the study was conducted, year of publication, detailed study design (i.e., parallel arms, cross-over or split-mouth), initial and final number of participants prior to and following dropouts, distribution of participants and/or sites across treatment groups, distribution of participant age and gender across treatment groups, type of rehabilitated edentulism (i.e., partial or complete), as well as time of functional loading, and follow-up time thereafter. Any missing data that could contribute to the scope of this systematic review were requested from the respective corresponding authors via electronic communication.

2.9 | Risk assessment

The risk of bias pertaining to each of the included studies was assessed by two authors (M.T. and G.A.) independently using the revised Cochrane Collaboration's tool for assessing risk of bias in randomized trials (RoB 2) (Sterne et al., 2019). Disagreements in the process were resolved by open discussion and consensus.

The following domains were assessed as follows:

- Risk of bias arising from the randomization process;
- Risk of bias due to deviations from the intended interventions (effect of assignment to intervention);
- Risk of bias due to deviations from the intended interventions (effect of adhering to intervention);
- Missing outcome data;
- Risk of bias in measurement of the outcome;

- Risk of bias in selection of the reported result.

Based on the overall risk of bias, included RCTs were categorized into low risk of bias, high risk of bias, or expressing some concerns, according to the following tailored criteria:

- *High risk of bias* if high risk of bias was identified for ≥1 domain
- *Some concerns* if the study presents some concerns for ≥3 domains
- *Low risk of bias* if low risk of bias was identified for ≥4 domains

2.9.1 | Data synthesis and summary of findings

Following article selection, Cohen's kappa coefficient (κ) was used to assess inter-examiner agreement. Data were organized into evidence tables, and a descriptive summary was done to check the quantity of data and study variations (i.e., study characteristics, quality, and outcomes). This aided in settling the likeness of studies and appropriateness of combining their individual outcomes into pooled estimates (i.e., meta-analysis). Continuous data were combined into random-effects meta-analyses where weighted mean differences (MD) with their associated 95% confidence intervals (CI) were calculated using a specific software (Review Manager 5 [RevMan 5], version 5.3. Copenhagen: Nordic Cochrane Center, The Cochrane Collaboration, 2014). The analyses were carried on using the generic inverse variance statistical method where the MD and standard error (SE) are entered for all studies, in order to accommodate data pooling from split-mouth and parallel-group studies in the meta-analysis, and facilitate data synthesis (Stedman, Curtin, Elbourne, Kesselheim, & Brookhart, 2011). For split-mouth trials, it was assumed an intra-cluster correlation coefficient of 0.05, while for parallel trials, a coefficient of 0 for the calculation of SE. The significance of discrepancies in the estimates of the treatment effects from the different trials was assessed by means of Cochrane's Q test for homogeneity and the I^2 statistic.

The GRADE approach was used to assess the quality of evidence corresponding to each outcome of interest reported in the included studies, and a summary of finding table was generated accordingly (Guyatt et al., 2011). The summary of finding table provides outcome-centered information on the quality of evidence (high, moderate, low, or very low quality) pertinent to the outcomes of interest and the study interventions' magnitude of effect based on

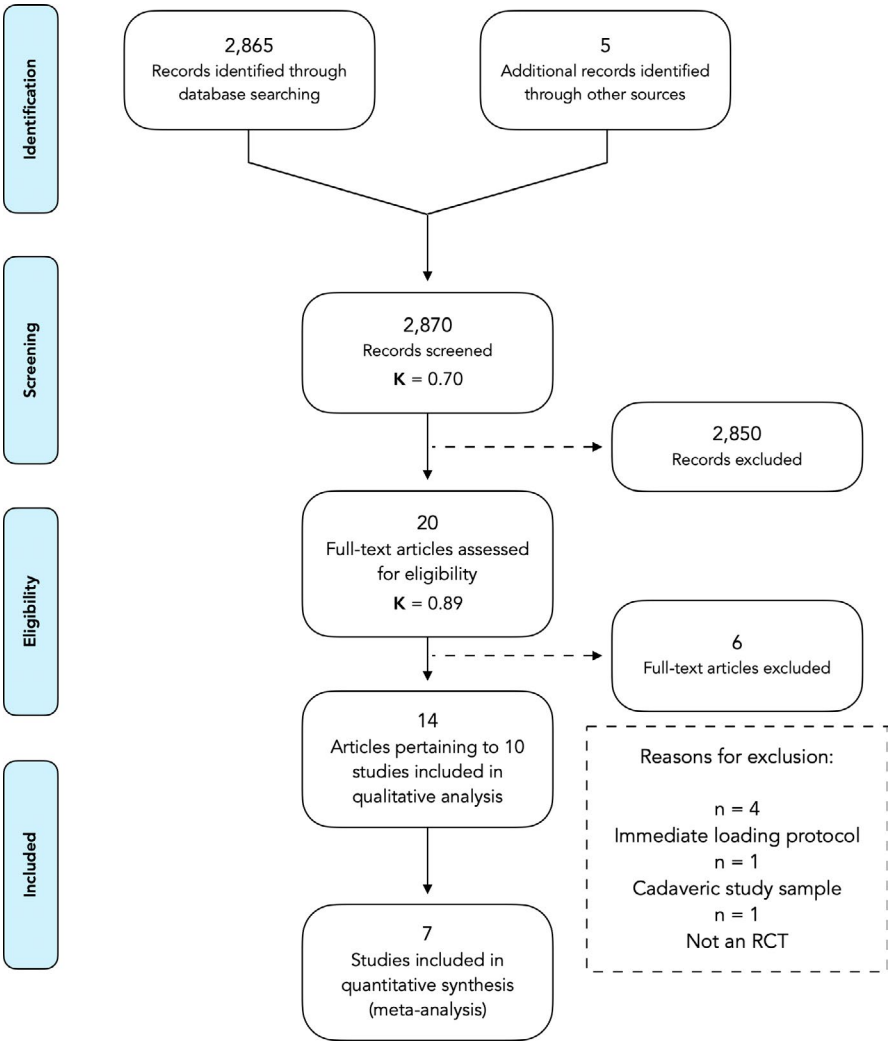

FIGURE 2 Flowchart illustrating the article selection process

TABLE 2 General characteristics and qualitative data of the included studies

Study Year of publication + Author(s)	Country	Study Design	Total Study Sample (After Dropouts)	Groups/ Interventions	Type of Guide Support Surgical Approach	Male/Female	Age	Type of Edentulism	Type of Edentulism & Arch Distribution
2006 Fortin et al.	France	RCT Parallel Arms Design	60 patients 152 implants	Control: Free-handed Implant Placement 30 patients	Open Flap Approach	18 Females/12 Males	20–79 years	Complete and Partial Edentulism	Not Reported
				Test: Computer-aided Implant Placement 30 patients"	Tooth- or Mucosa-supported Flapless Approach	20 Females/10 Males	19–82 years		
2010 Arisan et al.	Turkey	RCT Parallel Arms Design	52 patients 341 implants (6 to 8 implants per patient)	Control: Free-handed Implant Placement 21 patients	Open Flap Approach	Distribution in Total Population: Males: 25 Females: 27 (Specific allocation per group not reported)	Mean Age of Total Population: 48.4 years Range 28 to 63 years (Specific mean or range per group not reported)	Complete Edentulism	30 Maxillary/24 Mandibular (2 pts received surgery in both arches)
				Test 1: Computer-aided Implant Placement (Aytasarim-Classic System) 15 patients	Bone-supported Open Flap Approach				
				Test 2: Computer-aided Implant Placement (Materialise ©) 16 patients	Mucosa-supported Flapless Approach				
2013 Farley et al.	United States	RCT Split-Mouth Design	10 patients 20 implants (2 implants per patient)	Control: Partially guided Implant Placement (cast-based) 10 patients	Tooth-supported Open Flap Approach	5 Females/5 Males	Age Range of Total Population: 18–68 years (Mean and *SD* calculable from paper; Table 4)	Partial Edentulism	3 Maxillary/7 Mandibular (Single tooth sites with symmetrical distribution)
				Test: Computer-aided Implant Placement 10 patients					

Number of Implants Placed	Relevant Outcomes Measures	Healing period prior to implant loading: Specific or range	Total follow-up time: If applicable	Dropouts?	Complications	Summary of main findings	Source of funding and conflicts of interest (COI)
72 implants 80 implants	Patient-reported pain between day 0 and 6 postoperatively using a VAS Intake of analgesic medications	Not Reported	6 days following implant placement	0 (Not explicitly reported)	Edema in 13/30 patients Hematoma in 6/30 patients Edema in 2/30 patients Hematoma in 1/30 patients	The flapless, guided implant placement approach was associated with less immediate postoperative discomfort (up to 6 days). Also the average number of analgesic tablets was lower in the flapless group at all time points.	Not Reported
141 implants 99 implants 101 implants	Duration of surgical procedure Patient-reported pain between day 0 and 7 postoperatively using a VAS Facial swelling at day 2 and 6 postoperatively using a pre-determined scale Intake of analgesic medications Implant survival rate	2 to 4 months	4 months following implant placement	Not Reported	Trismus and postoperative bleeding was lower in the flapless group Hematoma was observed in none of patients in the MSG Group, in 9.5% of patients in the CPG Group and in 6.25% of patients in the BSG Group	Flapless implant placement using a mucosa-supported, computer-generated guide was associated with significantly less surgical time, less consumption of analgesics and less postoperative pain as compared to the other two groups. Implant failure at 4 months postoperatively was comparable between groups: 3 implants in MSG Group, 2 implants in BSG Group and 3 implants in CPG Group.	Supported by: Risus Medical (Turkish Branch of Thommen Medical, SPI) and Dentsply-Friadent COI: None
10 implants 10 implants	Discrepancy between planned and actual implant position	Not Reported	No follow-up (All measurements were obtained immediately after implant placement)	Not Reported	None	Single implants placed with computer-generated surgical guides were generally closer to the planned positions than those placed with conventional guides. However, statistically significant differences between groups were only observed in terms of linear horizontal deviation, in favor of the computer-guided group.	Supported by: Biomet 3i COI: None

(Continues)

TABLE 2 (Continued)

Study Year of publication + Author(s)	Country	Study Design	Total Study Sample (After Dropouts)	Groups/ Interventions	Type of Guide Support Surgical Approach	Male/Female	Age	Type of Edentulism	Type of Edentulism & Arch Distribution
2014 Vercruyssen et al. A/B/C	Belgium	RCT Parallel Arms Design	59 patients 314 implants (4 to 6 implants per patient)	Control: Free-handed Implant Placement	Open Flap Approach	8 Females/4 Males	39–72 years	Complete Edentulism	3 Maxillary/9 Mandibular
				Test 1: Computer-aided Implant Placement (Materialise ©)	Mucosa-supported Flapless Approach	7 Females/5 Males	38–78 years		6 Maxillary/6 Mandibular
				Test 2: Computer-aided Implant Placement (Materialise ©)	Bone-supported Open Flap Approach	8 Females/4 Males	31–72 years		9 Maxillary/3 Mandibular
				Test 3: Computer-aided Implant Placement (Facilitate ™)	Mucosa-supported Flapless Approach	6 Females/6 Males	46–74 years		7 Maxillary/5 Mandibular
				Test 4: Computer-aided Implant Placement (Facilitate™)	Bone-supported Open Flap Approach	8 Females/4 Males	43–65 years		6 Maxillary/6 Mandibular
				Test 5: Partially guided Implant Placement (cast-based; pilot drill only)	Tooth-supported Open Flap Approach	4 Females/8 Males	40–75 years		8 Maxillary/4 Mandibular
2015 Shen et al.	China	RCT Parallel Arms Design	60 patients 109 implants	Control: Free-handed Implant Placement 30 patients	Open Flap Approach	16 Females/14 Males	Mean Age of Total Population: 40 years (no *SD* reported) Age range: 22–64 years (Specific mean or range per group not reported)	Complete and Partial Edentulism	Not Reported
				Test: Computer-aided Implant Placement 30 patients	Tooth-supported Flapless Approach	18 Females/12 Males			

Number of Implants Placed	Relevant Outcomes Measures	Healing period prior to implant loading: Specific or range	Total follow-up time: If applicable	Dropouts?	Complications	Summary of main findings	Source of funding and conflicts of interest (COI)
51 implants 55 implants 53 implants 52 implants 52 implants 51 implants	Publication A: Discrepancy between planned and actual implant position Publication B: Duration of the surgical procedure. Pain as measured with a VAS and the McGill Pain Questionnaire, and the number of postoperative analgesics taken Publication C: Implant survival, PD, BOP, Plaque indices and marginal bone levels at 1 year after delivery of final prosthesis	3 to 4 months	Publication C only: 1 year following delivery of the final prosthesis	0 0 1 0 0 0	Not Reported	Publication A: Computer-guided protocols are more precise than mental navigation or surgical placement of dental implants using an analogic guide Publication B: No significant differences between groups were observed in terms of reported pain and intake of analgesics, although there was tendency toward worse outcomes in the groups that underwent flap surgery Publication C: No significant differences in terms of implant survival (no implant failed in the study), clinical peri-implant parameters and marginal bone level changes were observed between groups	Supported by: Astra Tech Company (Mölndal, Sweden) and Materialise Dental Company (Leuven, Belgium) COI: None
52 implants 57 implants	Discrepancy between planned and actual implant position	6 months	12 months following implant placement	0 0	Not Reported	Accuracy was higher in the computer-guided group for all the parameters analyzed. All observations reached statistical significance, except for implant depth.	Supported by: the National Natural Science Foundation of China, Shanghai Leading Academic Discipline Project, Natural Science Foundation of Shanghai Municipality, Science and Technology Commission of Shanghai Municipality Science Research Project COI: None

(Continues)

TABLE 2 (Continued)

Study Year of publication + Author(s)	Country	Study Design	Total Study Sample (After Dropouts)	Groups/ Interventions	Type of Guide Support Surgical Approach	Male/Female	Age	Type of Edentulism	Type of Edentulism & Arch Distribution
2018 Younes et al.	Belgium	RCT Parallel Arms Design	32 patients 71 implants (≥ 2 implants per patient)	Control: Free-handed Implant Placement 11 patients	Open Flap Approach	8 Females/3 Males	Mean: 57 years (SDs were not reported)	Partial Edentulism	Maxillary arches only
				Test 1: Partially guided Implant Placement (3D-printed; pilot drill only) 11 patients	Tooth-supported Flapless Approach	7 Females/4 Males	Mean: 54 years (SDs were not reported)		
				Test 2: Computer-aided Implant Placement 10 patients	Tooth-supported Flapless Approach	6 Females/4 Males	Mean: 60 years (SDs were not reported)		
2018 Schneider et al. 2019 Sancho-Puchades et al. 2019 Schneider et al.	Switzerland	RCT Parallel Arms Design	57 patients 73 implants	Control: Free-handed Implant Placement 26 patients	Open Flap Approach	Not Reported	Not Reported	Partial Edentulism	Not Reported
				Test 1: Computer-aided Implant Placement with Stereolithographic Guide & Metallic Sleeve 24 patients	Tooth-supported Open Flap Approach				
				Test 2: Computer-aided Implant Placement with 3D-printed Guide & No Metallic Sleeve 23 patients	Tooth-supported Open Flap Approach				

Number of Implants Placed	Relevant Outcomes Measures	Healing period prior to implant loading: Specific or range	Total follow-up time: If applicable	Dropouts?	Complications	Summary of main findings	Source of funding and conflicts of interest (COI)
26 implants 24 implants	Discrepancy between planned and actual implant position in terms	3 months	12 weeks following implant placement	0 0	Not Reported	Significant difference in accuracy between both guided groups and the free-handed group. The highest accuracy for the fully guided and the lowest accuracy for the free-handed.	Supported by: Dentsply Implants (Mölndal, Sweden) COI: One of the authors reported a collaboration agreement with Nobel Biocare (Götheborg, Sweden)
21 implants				1 patient was still included in the Fully Guided Group despite the operator's use of mental navigation for placement (as per intention-to-treat principle) 1 patient dropped out prior to surgery			
26 implants 24 implants 23 implants	Series Part 1: Implant survival rate Series Part 2: patient-reported discomfort on a VAS scale and an open-answer questionnaire. Series Part 4: Discrepancy between planned and actual implant position	Not Reported	2 weeks following prosthetic delivery	0 (Not explicitly reported)	(According to part 2) Postoperative complications (hematoma, limited mouth opening etc.) did occur, however, raw data detailing number and/or nature of occurrences was not reported.	Computer-assisted implant planning and placement possess higher diagnostic potential than conventional methods. Patients generally prefer computer-based methods, however, there is no significant difference in intra- or postoperative discomfort compared to conventional methods. Computer-assisted implant planning and placement provides higher accuracy and precision compared to conventional methods, though a safety margin and intra-surgical verification is still necessary in successfully performing computer-assisted methods.	Supported by: Dentsply and Swissmeda COI: None

(Continues)

TABLE 2 (Continued)

Study Year of publication + Author(s)	Country	Study Design	Total Study Sample (After Dropouts)	Groups/ Interventions	Type of Guide Support Surgical Approach	Male/Female	Age	Type of Edentulism	Type of Edentulism & Arch Distribution
2019 Smitkarn et al.	Thailand	RCT Parallel Arms Design	52 patients 60 implants	Control: Free-handed Implant Placement 26 patients	Open Flap Approach	Not Reported	Not Reported	Partial Edentulism	39 Maxillary/21 Mandibular
				Test: Computer-aided Implant Placement 26 patients	Tooth-supported Open Flap Approach				
2020 Magrin et al.	Brazil	RCT Split-Mouth Design	12 patients 24 implants	Control: Partially guided Implant Placement (cast-based) 12 patients	Open Flap Approach	11 Females/1 Male	Mean Age of Total Population: 42 ± 6.01 years	Partial Edentulism	Mandibular Arches Only (Single tooth sites with symmetrical distribution)
				Test: Computer-aided Implant Placement 12 patients	Tooth-supported Flapless Approach				
2020 Varga et al.	Hungary	RCT Parallel Arms Design	101 patients 207 implants	Control: Free-handed Implant Placement 26 patients	Open Flap Approach	13 Females/13 Males	40.38 ± 7.15 years	Partial Edentulism	18 Maxillary/37 Mandibular
				Test 1: Partially guided Implant Placement (3D-printed; pilot drill only) 23 patients	Tooth-supported Not Reported	15 Females/8 Males	41.96 ± 7.49 years		20 Maxillary/29 Mandibular
				Test 2: Partially guided Implant Placement (3D-printed; pilot drill & osteotomy preparation only) 24 patients	Tooth-supported Not Reported	10 Females/14 Males	40.63 ± 9.23 years		17 Maxillary/34 Mandibular
				Test 3: Computer-aided Implant Placement 28 patients	Tooth-supported Not Reported	13 Females/15 Males	42.11 ± 8.23 years		15 Maxillary/37 Mandibular

Number of Implants Placed	Relevant Outcomes Measures	Healing period prior to implant loading: Specific or range	Total follow-up time: If applicable	Dropouts?	Complications	Summary of main findings	Source of funding and conflicts of interest (COI)
30 implants (22 patients = 1 implant; 4 patients = 2 implants)	Discrepancy between planned and actual implant position	Not Reported	2 weeks following implant placement	0	Not Reported	sCAIP provides greater accuracy than freehand placement in a single edentulous space.	No external funding COI: None
30 implants (22 patients = 1 implant; 4 patients = 2 implants)				0			
12 implants	Discrepancy between planned and actual implant position Pain, discomfort, swelling bleeding & ecchymosis as measured with a VAS.	Not Reported	6 days following implant placement	4 (2 of which were excluded due technical, intraoperative complications) Only 9 of 12 agreed to contribute to the PROMs.	Fracture of the buccal bone plate during implant insertion in one (test) site. No postoperative biological complications reported.	The discrepancy between planned and actual implant position for sCAIP was slightly less, in one aspect of deviation, than free-handed implant placement. PROMs were comparable between the treatment modalities.	One of the authors holds a declared scholarship (Coordination for Improvement of Higher Education Personnel – CAPES) COI: None
12 implants							
55 implants	Discrepancy between planned and actual implant position	Not Reported	No follow-up (All measurements were obtained immediately after implant placement)	5	Not Reported	All variations of sCAIP were significantly more accurate than free-handed implant placement; showing increasing accuracy with increasing guidance.	Supported by: a federal research grant (GINOP, Hungary) COI: Two of the authors reported being CEO and chief researcher of dicomLAB (Szeged, Hungary); the manufacturer of the sCAIP system in this study.
49 implants				7			
51 implants				5			
52 implants				3			

the available data. Due to this review only comprising RCTs, all the included studies started at high quality. The quality was then downgraded upon encountering evidence of: (1) limitations in study design (risk of bias); (2) inconsistency (heterogeneity); (3) indirectness; (4) imprecision; and/or (5) publication bias.

3 | RESULTS

3.1 | Literature selection process

The initial search yielded a total of 2,865 entries, of which 2,158 were found in PubMed, 419 in EMBASE, and 288 in CENTRAL. Five additional articles were identified through hand searching. After title and abstract screening, a total of 20 articles were selected for full-text review. Six of these articles were excluded after full-text review, the reasons for which are summarized in Figure 2 and displayed in Table S1, under supplementary materials. Thus, the final selection comprised a total of 14 articles (Arisan, Karabuda, & Ozdemir, 2010; Farley, Kennedy, McGlumphy, & Clelland, 2013; Fortin, Bosson, Isidori, & Blanchet, 2006; Magrin et al., 2020; Sancho-Puchades et al., 2019; Schneider, Sancho-Puchades, Benic, Hammerle, & Jung, 2018; Schneider et al., 2019; Shen et al., 2015; Smitkarn, Subbalekha, Mattheos, & Pimkhaokham, 2019; Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, Coucke, & Quirynen, 2014; Vercruyssen, van de Wiele, et al., 2014; Younes et al., 2018). Kappa scores for inter-examiner agreement for title and abstract review as well as full-text review were 0.70 and 0.89, respectively. The entire article selection process is displayed in Figure 2.

3.2 | Characteristics of the included studies

The overall characteristics of the fourteen included articles, that stemmed from ten RCTs, are outlined in Table 2. Eight of the included articles represented the outcomes of a single clinical trial each (Arisan et al., 2010; Farley et al., 2013; Fortin et al., 2006; Magrin et al., 2020; Shen et al., 2015; Smitkarn et al., 2019; Varga et al., 2020; Younes et al., 2018), whereas the remaining six articles reported different outcomes of interest pertaining to the population enrolled in two RCTs (Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014).

3.2.1 | Study design

As aforementioned, all the selected articles reported the outcomes of a total of 10 RCTs (Arisan et al., 2010; Farley et al., 2013; Fortin et al., 2006; Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Shen et al., 2015; Smitkarn et al., 2019; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014; Younes et al., 2018). Two of the RCTs had a split-mouth design (Farley et al., 2013; Magrin et al., 2020), while all the remaining studies had a parallel study arms design (Arisan et al., 2010; Fortin et al., 2006; Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Shen et al., 2015; Smitkarn et al., 2019; Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014; Younes et al., 2018); five of the latter studies included two or more experimental groups (Arisan et al., 2010; Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014; Younes et al., 2018).

3.2.2 | Population and clinical scenarios

The number of dropouts was reported in seven of the ten studies (Arisan et al., 2010; Magrin et al., 2020; Shen et al., 2015; Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014; Younes et al., 2018). One patient dropped out of one study with a total sample of 59 patients and 314 implants (Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014) and another patient dropped out of a second study with a total sample of 32 patients and 71 implants (Younes et al., 2018). The latter of the two had also retained the data of one patient who received the implant via FHIP, despite the randomization for that patient dictating fully guided implant placement. The reason for this protocol deviation is that the guide was not delivered on time by the manufacturer. Another study with a total sample of 12 patients reported a dropout of 4 patients, 2 of which were due to intraoperative complications and 2 due to unspecified dropout following enrollment (Magrin et al., 2020). In the same study, only 9 of the final 12 enrolled patients agreed to contribute to the PROMs. While Schneider et al. (2019) reported the exclusion of 19 cases from data analysis due to intraoperative deviation from the computer-aided placement protocol, the overall data analysis including those cases was still reported (Schneider et al., 2019). In most of the included studies, the attrition rate was either minimal or accounted for during data analysis and, therefore, unlikely to impact the reliability of the data. However, one study with a total sample of 101 patients had reported a dropout of 20 patients who were immediately excluded without reporting information on their randomized intervention assignments and/or an appropriate analysis to estimate the effect of intervention adherence (Varga et al., 2020). This was considered in the risk of bias assessment.

Recipient arch distribution and characteristics varied between the included studies. Six studies included partially edentulous arches only (Farley et al., 2013; Magrin et al., 2020; Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Smitkarn et al., 2019; Varga et al., 2020; Younes et al., 2018), two included completely edentulous arches exclusively (Arisan et al., 2010;

Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014), and two other studies involved the treatment of both the former and the latter (Fortin et al., 2006; Shen et al., 2015). Of these, one study comprised implants placed in the maxillary arch only (Younes et al., 2018) and another in the mandibular arch only (Magrin et al., 2020). Five other studies specified that implants were placed in both arches (Arisan et al., 2010; Farley et al., 2013; Smitkarn et al., 2019; Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014) and the remaining three studies did not report arch distribution (Fortin et al., 2006; Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Shen et al., 2015).

3.2.3 | Treatment approaches

The control therapy, which consisted of FHIP or PGIP in all studies, was performed via an open flap approach. This was also the case with all the included sCAIP groups employing bone-supported surgical guides (Arisan et al., 2010; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014). Meanwhile, all the experimental treatment involving sCAIP and mucosa-supported surgical guides was performed via a flapless approach (Arisan et al., 2010; Fortin et al., 2006; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014). As for the experimental treatments performed using tooth-supported surgical guides, two studies reported that the procedure was done with an open flap (Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Smitkarn et al., 2019), while four studies followed a flapless approach (Farley et al., 2013; Magrin et al., 2020; Shen et al., 2015; Younes et al., 2018) and one study did not report this information (Varga et al., 2020). Furthermore, PGIP implant placement was included as an additional experimental group in three studies (Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014; Younes et al., 2018) and as the control group in another two (Farley et al., 2013; Magrin et al., 2020).

3.2.4 | Follow-up time

Overall, the median follow-up time among the included studies was 12 weeks (range: 1–48 weeks). The disparity in observational period duration between the included studies can be primarily attributed to individual study protocol guidelines, depending on their individual outcome measures of interest. Two studies, assessing accuracy only, had no follow-up past an evaluation immediately after implant placement (Farley et al., 2013; Varga et al., 2020). Fortin et al., Sancho-Puchades et al., and Magrin et al. evaluated PROMs at a postoperative follow-up of 6, 7, and 6 days, respectively (Fortin et al., 2006; Magrin et al., 2020; Sancho-Puchades et al., 2019). Accuracy reported by Schneider et al. only required postoperative evaluation immediately following implant placement (Schneider et al., 2019), whereas survival rate follow-up was only stated as 2 weeks following implant loading with no mention of the loading protocol (Schneider et al., 2018). Similar to other PROM-reporting studies, Smitkarn and coworkers performed a postoperative computed tomography just 2 weeks after, and that marked the end of the study (Smitkarn et al., 2019). Younes et al. reported accuracy of placement 3 months following surgery, at implant loading (Younes et al., 2018). Arisan et al. reported on implant survival and associated PROMs at 4 months postoperatively (Arisan et al., 2010). Finally, both Vercruyssen et al. and Shen et al. reported several outcomes over a 12-month observational period, differing in baseline between implant placement (Shen et al., 2015) and implant loading (Vercruyssen, van de Wiele, et al., 2014).

3.3 | Quality of the evidence and risk of bias assessment

According to the revised Cochrane Collaboration's tool for assessing risk of bias in randomized trials (RoB 2), five studies exhibited a low risk of bias (Arisan et al., 2010; Magrin et al., 2020; Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014; Younes et al., 2018) and the remaining five exhibited a high risk of bias (Farley et al., 2013; Fortin et al., 2006; Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Shen et al., 2015; Smitkarn et al., 2019) as shown in Figure 3. Potential biases associated with measurement of the outcome were the most commonly encountered.

The GRADE ratings pertaining to the outcome-centered quality of the evidence and pooled summary estimates (where applicable) have been outlined in the summary of findings table (Table 3). The overall quality concerning comparisons between interventions for the 4 assessed outcomes of interest ranged between very low and high quality of evidence.

3.4 | Qualitative assessment of outcomes

The extracted data, pertaining to the outcomes of interest, are displayed in Table 4.

3.4.1 | Clinical outcomes

Implant survival and success rates

Implant success rate was not reported in any of the ten included studies, whereas four studies did report the implant survival rate (Arisan et al., 2010; Schneider et al., 2018; Shen et al., 2015; Vercruyssen, van de Wiele, et al., 2014). One of these studies reported 4-month survival rates of 96.97%–98.02% for all study groups (Arisan et al., 2010).

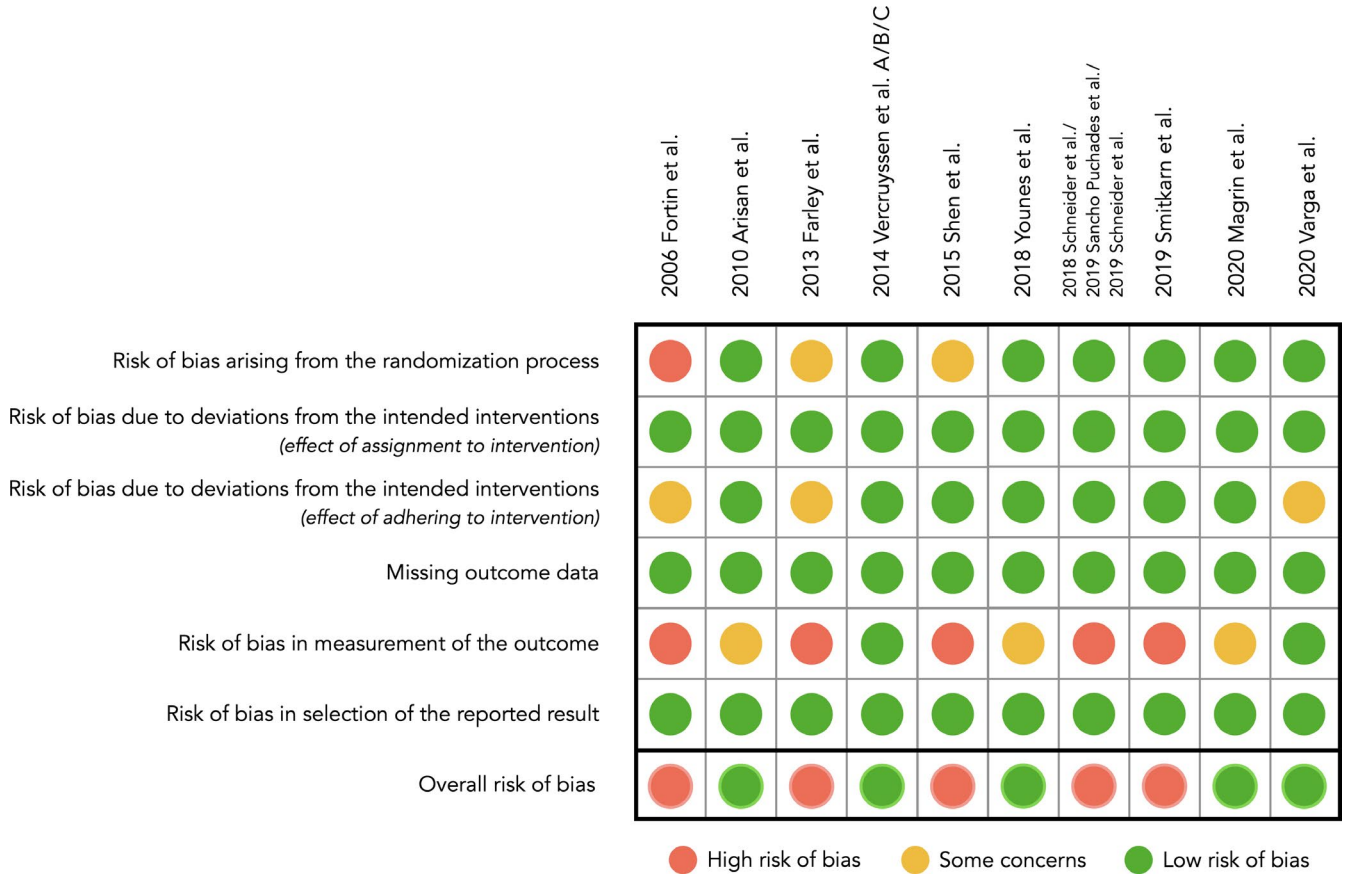

FIGURE 3 Risk of bias of included studies

Meanwhile, two studies reported 12-month survival rates of 100% pertaining to all study groups (Shen et al., 2015; Vercruyssen, van de Wiele, et al., 2014). The remaining study reported a 2-week implant survival rate of 100% for all groups. Furthermore, the loading protocol was not specified, and therefore, the survival timeline could not be determined (Schneider et al., 2018). Overall, the reported survival rates within all the individual studies did not differ significantly between the FHIP, PGIP, and sCAIP protocols. Due to inconsistency associated with the data concerning survival rate, the quality of evidence was considered at low quality.

3.4.2 | Digital outcomes

Accuracy of implant placement

Comparisons regarding implant placement accuracy or deviation from the planned position, between sCAIP and FHIP, were reported in six studies (Schneider et al., 2019; Shen et al., 2015; Smitkarn et al., 2019; Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Younes et al., 2018) and between sCAIP and PGIP in two studies (Farley et al., 2013; Magrin et al., 2020). Three of the former studies reported on the accuracy of PGIP also (Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Younes et al., 2018). All of these studies reported on the angular and 3D bodily deviation between the planned and final implant position. The angular deviation values demonstrated were generally greater in free-handed (6.90 ± 4.40° to 9.92 ± 6.01°) than partially guided (3.50 ± 1.60° to 8.43 ± 5.10°) and computer-aided (2.20 ± 1.10° to 5.95 ± 0.87°) implant placement. The 3D bodily deviations exhibited a less drastic but similar pattern between free-handed (coronal: 1.25 ± 0.62 to 2.77 ± 1.54 mm; apical: 2.10 ± 1.00 to 2.91 ± 1.52 mm), partially guided (coronal: 1.12 ± 0.10 to 2.97 ± 1.41 mm; apical: 1.43 ± 0.18 to 3.40 ± 1.68 mm), and computer-aided (coronal: 0.54 ± 0.33 to 2.34 ± 1.01 mm; apical: 0.90 ± 0.43 to 2.53 ± 1.11 mm) implant placement. Meanwhile, only two studies reported on depth deviation, as well (Shen et al., 2015; Younes et al., 2018). For all the aforementioned measures of implant placement accuracy, sCAIP produced consistently superior outcomes to FHIP and PGIP implant placement. However, in the only study that reported depth deviation for all three protocols, the respective values were non-significantly greater in the partially guided (0.68 ± 0.09 mm) versus free-handed (0.50 ± 0.09 mm) implant placement, which were both greater than the sCAIP (0.43 ± 0.09 mm) (Younes et al., 2018).

Marginal bone level

Differences in marginal bone level changes between the different modalities were only reported in one of the included studies (Vercruyssen, van de Wiele, et al., 2014). MBL changes between free-handed, partially guided and computer-aided implant placement in this study were both clinically and statistically comparable

TABLE 3 Summary of finding table with the GRADE approach quality of the evidence assessment

Navigation-related approach to dental implant placement Population: **Patients in need of ≥1 dental implant(s) for tooth replacement.** Intervention: **Static computer-aided implant placement (sCAIP)** Comparison: **Free-handed or partially guided implant placement**						
Outcomes	**Summary Estimates (WMD [95% CI] *P* value)**	**Favors**	**Heterogeneity (I^2; %)**	**No of Participants/ Implants (studies)**	**Quality of the Evidence (GRADE)**	**Comments**
Accuracy of Placement				383/878 (8)	⊕⊕⊕⊕ high	A similar trend in statistically significant summary estimates, but to a lesser magnitude, was demonstrated between sCAIP and partially guided implant placement for angular deviation only. [c]
Angular Deviation (degrees) (follow-up: N/A)	4.41 [3.99,4.83][a] $p < .00001$ 4.37 [3.98,4.76][b] $p < .0001$	sCAIP	84			
Coronal Deviation (mm) (follow-up: N/A)	0.65 [0.50,0.79][a] $p < .00001$ 0.63 [0.49,0.78][b] $p < .00001$	sCAIP	99			
Apical Deviation (mm) (follow-up: N/A)	1.13 [0.92,1.34][a] $p < .00001$ 1.11 [0.91,1.32][b] $p < .00001$	sCAIP	97			
MBL Changes (mm) (follow-up: 12 months)	See comment	NA	NA	59/314 (1)	⊕ very low	Difference is uncertain [d]
Survival Rate (%) (follow-up: 4–12 months) [e]	See comment	NA	NA	228/837 (4)	⊕ low	Difference is uncertain [f]
PROMs: Postoperative Pain/Morbidity VAS Scores. Scale from 1 to 10 or 1 to 100.[g] (follow-up: 6–7 days)	See comment	NA	NA	240/904 (5)	⊕⊕ low	Difference is uncertain [h]

Abbreviations: CI, Confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MBL, Marginal bone level; NA, Not applicable; PROMs, Patient-reported outcome measures; VAS, Visual analogue scale; WMD, Weighted mean difference.

GRADE Working Group grades of evidence:

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

[a]Results of meta-analyses including the first of two eligible test groups from one study (Figures 4 and 5).

[b]Results of meta-analyses including the second of two eligible test groups from one study (Figures 4 and 5).

[c]Refer to Figures 4 and 5 for the pertinent forest plots.

[d]An insufficient number of studies precluded elaborate analysis.

[e]One study reported a 2-week follow-up examination after prosthetic delivery without detailing their loading protocol.

[f]Heterogeneity in therapeutic approach and follow-up period precluded data pooling.

[g]Three studies used a scale from 1 to 10 and two studies used a scale from 1 to 100.

[h]Heterogeneity in therapeutic approach precluded data pooling.

TABLE 4 Quantitative data of included studies pertaining to the outcomes of interest

Study	Implant survival rate	Implant success rate	Radiographic marginal bone level change	Linear or angular implant placement deviation	Patient-centered outcomes
Year of publication + Author(s)	%	%	mm	Degrees and/or mm	Pain/Discomfort, QoL outcomes, etc…
2006 Fortin et al.	Not Reported	Not Reported	Not Reported	Not Reported	Pain VAS (0–10): Significantly lower scores in flapless, guided implant placement group as compared to conventional placement during the first 6 days postoperatively (Only ranges at different time points were reported)
2010 Arisan et al.	At 4 months postoperatively MSG Group = 96.97% BSG Group = 98.02% CPG Group = 97.88%	Not Reported	Not Reported	Not Reported	Pain VAS (0–10): Significantly lower pain scores in the flapless, guided implant placement group as compared to open flap, bone-supported guided implant placement and conventional placement on the day of the surgical procedure (Numeric data not reported)
2013 Farley et al.	Not Reported	Not Reported	Not Reported	Control Group: Angular deviation: 6.13 ± 4.04° Coronal deviation: 1.99 ± 1.00 mm Apical deviation: 2.54 ± 1.23 mm Test Group: Angular deviation: 3.68 ± 2.19° Coronal deviation: 1.45 ± 0.60 mm Apical deviation: 1.82 ± 0.60 mm	Not Reported

(Continues)

TABLE 4 (Continued)

Study	Implant survival rate	Implant success rate	Radiographic marginal bone level change	Linear or angular implant placement deviation	Patient-centered outcomes
Year of publication + Author(s)	%	%	mm	Degrees and/or mm	Pain/Discomfort, QoL outcomes, etc…
2014 Vercruyssen et al. (A, B & C)	100% at 1 year after prosthesis delivery in all groups	Not Reported	Difference between implant placement and 1 year post-loading Group 1:0.03 ± 0.34 mm Group 2: −0.04 ± 0.40 mm Group 3:0.07 ± 0.35 mm Group 4:0.11 ± 0.24 mm Group 5:0.02 ± 0.27 mm Group 6:0.01 ± 0.48 mm	Control Group: Angular deviation: 9.92 ± 6.01° Coronal deviation: 2.77 ± 1.54 mm Apical deviation: 2.91 ± 1.52 mm Test Group 1: Angular deviation: 2.86 ± 1.60° Coronal deviation: 1.23 ± 0.60 mm Apical deviation: 1.57 ± 0.71 mm Test Group 2: Angular deviation: 3.79 ± 2.36° Coronal deviation: 1.60 ± 0.92 mm Apical deviation: 1.65 ± 0.82 mm Test Group 3: Angular deviation: 2.71 ± 1.36° Coronal deviation: 1.38 ± 0.64 mm Apical deviation: 1.60 ± 0.70 mm Test Group 4: Angular deviation: 3.20 ± 2.70° Coronal deviation: 1.33 ± 0.82 mm Apical deviation: 1.50 ± 0.72 mm Test Group 5: Angular deviation: 8.43 ± 5.10° Coronal deviation: 2.97 ± 1.41 mm Apical deviation: 3.40 ± 1.68 mm	Pain VAS (0–100): Detailed values at different time points during the first 7 days after implant placement for each group displayed in Table 3 of the original publication (; Vercruyssen, van de Wiele, et al., 2014). Nevertheless, the summary of findings is that no significant differences between groups were observed during the observational period in terms of intake of analgesics, reported pain and quality of life outcomes
2015 Shen et al.	100% at 12 months after implant placement in both groups	Not Reported	Not Reported	Control Group: Angular deviation 8.84 ± 4.64° Coronal deviation 2.07 ± 0.51 mm Apical deviation 2.89 ± 1.02 mm Depth deviation 0.78 ± 0.33 mm Test Group: Angular deviation 4.21 ± 1.91° Coronal deviation 1.18 ± 0.72 mm Apical deviation 1.43 ± 0.74 mm Depth deviation 0.54 ± 0.29 mm	Not Reported

(Continues)

TABLE 4 (Continued)

Study Year of publication + Author(s)	Implant survival rate %	Implant success rate %	Radiographic marginal bone level change mm	Linear or angular implant placement deviation Degrees and/or mm	Patient-centered outcomes Pain/Discomfort, QoL outcomes, etc…
2018 Younes et al.	Not Reported	Not Reported	Not Reported	Control Group: Angular deviation 6.99 ± 0.87° Coronal deviation 1.45 ± 0.10 mm Apical deviation 2.11 ± 0.18 mm Depth Deviation 0.50 ± 0.09 mm Test Group 1: Angular deviation 5.95 ± 0.87° Coronal deviation 1.12 ± 0.10 mm Apical deviation 1.43 ± 0.18 mm Depth Deviation 0.68 ± 0.09 mm Test Group 2: Angular deviation 2.30 ± 0.92° Coronal deviation 0.73 ± 0.10 mm Apical deviation 0.97 ± 0.19 mm Depth Deviation 0.43 ± 0.09 mm	Not Reported
4-Part Publication Series: 2018 Schneider et al. 2019 Sancho-Puchades et al. 2019 Schneider et al. (A & B)	100% at 2 weeks following prosthetic delivery in all groups	Not Reported	Not Reported	Control Group: Angular deviation 7.36 ± 3.36° Coronal deviation 1.25 ± 0.62 mm Apical deviation 2.32 ± 1.24 mm Test Group 1: Angular deviation 2.41 ± 1.40° Coronal deviation 0.54 ± 0.33 mm Apical deviation 0.90 ± 0.43 mm Test Group 2: Angular deviation 2.69 ± 1.78° Coronal deviation 0.61 ± 0.27 mm Apical deviation 1.02 ± 0.64 mm	After treatment, 50% of control group patients, 76% of T1 group patients and 94% of T2 group patients, were satisfied with their allocation. The duration of surgery perceived by the patients did not significantly differ from the actual surgical duration. VAS scores (0–100): Significantly higher intraoperative pain and discomfort associated with longer surgeries, and higher immediate postoperative pain with two surgical sites and two separate flaps. Postoperative morbidity (up to 7 days) was statistically comparable between groups. (Numeric data not reported)

(Continues)

TABLE 4 (Continued)

Study	Implant survival rate	Implant success rate	Radiographic marginal bone level change	Linear or angular implant placement deviation	Patient-centered outcomes
Year of publication + Author(s)	%	%	mm	Degrees and/or mm	Pain/Discomfort, QoL outcomes, etc…
2019 Smitkarn et al.	Not Reported	Not Reported	Not Reported	Control Group: Angular deviation 6.90 ± 4.40° Coronal deviation 1.50 ± 0.70 mm Apical deviation 2.10 ± 1.00 mm Test Group: Angular deviation 3.10 ± 2.30° Coronal deviation 1.00 ± 0.60 mm Apical deviation 1.30 ± 0.60 mm	Not Reported
2020 Magrin et al.	Not Reported	Not Reported	Not Reported	Control Group: Angular deviation 3.50 ± 1.60° Coronal deviation 1.93 ± 0.95 mm Apical deviation 2.19 ± 1.00 mm Test Group: Angular deviation 2.20 ± 1.10° Coronal deviation 2.34 ± 1.01 mm Apical deviation 2.53 ± 1.11 mm	Pain VAS (0–10): Detailed values per item in the questionnaire completed after implant placement for each group displayed in Table 3 of the original publication (Magrin et al., 2020). Nevertheless, the summary of findings is that no significant differences were identified for any of the questionnaire items between the two groups
2020 Varga et al.	Not Reported	Not Reported	Not Reported	Control Group: Angular deviation: 7.03 ± 3.44° Coronal deviation: 1.82 ± 0.94 mm Apical deviation: 2.43 ± 0.98 mm Test Group 1: Angular deviation: 5.71 ± 3.68° Coronal deviation: 1.57 ± 0.91 mm Apical deviation: 1.86 ± 1.09 mm Test Group 2: Angular deviation: 4.30 ± 3.33° Coronal deviation: 1.37 ± 0.79 mm Apical deviation: 1.59 ± 0.86 mm Test Group 3: Angular deviation: 3.04 ± 1.51° Coronal deviation: 1.40 ± 0.54 mm Apical deviation: 1.59 ± 0.59 mm	Not Reported

between groups. Due to an insufficient body of evidence associated with the data concerning marginal bone level changes, the quality of evidence was considered at very low quality.

3.4.3 | Patient-reported outcome measures

Five of the included studies reported PROMs (Arisan et al., 2010; Fortin et al., 2006; Magrin et al., 2020; Sancho-Puchades et al., 2019; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014), primarily assessing intraoperative and/or postoperative pain, among other patient-centered factors (Tables 2, 4). While two of the studies reported much less pain, recorded by means of a visual analogue scale (VAS), associated with computer-aided implant placement (Arisan et al., 2010; Fortin et al., 2006), three reported pain to be comparable between different modalities (Magrin et al., 2020; Sancho-Puchades et al., 2019; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014). Alternative methods for pain assessment reported in one of the studies were a quantitative evaluation of painkillers consumed following a procedure and the Dutch version of the McGill Pain Questionnaire (MPQ-DLV) (Vercruyssen, De Laat, et al., 2014). Similar to the VAS results, these methods demonstrated no difference in pain severity and duration between treatment approaches. The same RCT had also included quality of life outcome measures, based on the oral health-related quality of life (OHIP-49) and health-related quality of life (HRQOL) instruments, reporting no perceived difference between patients in all study groups with the former instrument, but minimal difference with the latter (Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014). The HRQOL revealed a significant difference in the quality of life at postoperative days 1 and 2 between mucosa- and bone-supported surgical guide study groups, in favor of mucosa-supported guides. Significant differences were also observed between the mucosa-supported surgical guide and FHIP study groups at day 1, also in favor mucosa-supported guides. Due to an inconsistency and a particularly relevant limitation in study design (potential risk of bias in outcome assessment blinding) associated with the data concerning PROMs, the quality of evidence was considered at low quality.

3.5 | Quantitative assessment of outcomes

A meta-analysis was performed only if a minimum of 3 studies had performed a comparison of an outcome of interest between FHIP or PGIP and a static computer-aided counterpart that was comparable in the type of guide support (i.e., tooth-, mucosa-, or bone-supported). Seven of the ten included studies were eligible for inclusion into a pooled quantitative analysis, all of which utilized tooth-supported surgical guides (Farley et al., 2013; Magrin et al., 2020; Schneider et al., 2019; Shen et al., 2015; Smitkarn et al., 2019; Younes et al., 2018). The data from these seven allowed for the conduction of four quantitative analyses comparing accuracy of sCAIP versus FHIP or sCAIP versus PGIP.

The comparisons rendered by these analyses consisted of two deviation parameters, namely angular and 3D bodily deviation, assessing the accuracy of implant placement. Due to insufficient homogenous reporting by the included—and overall available—studies, a meta-analysis of depth deviation could not be performed. These sub-analyses are depicted in forest plots (Figures 4 and 5).

One of the studies included in the quantitative analyses had reported datasets pertaining to two test groups that may be considered sCAIP, differing in the manufacturing mode of the surgical guide and the presence of a metallic sleeve (Schneider et al., 2019). Another trial included one free-handed, two partially guided, and one static computer-aided implant placement group (Varga et al., 2020). Thus, to attain comprehensive data synthesis on the comparability of accuracy between the treatment modalities, a corresponding pair of meta-analyses was conducted considering each PGIP or sCAIP group separately.

Although a limitation in study design attributed to potential risk of bias in one domain (measurement of the outcome) was commonly demonstrated, the quality of evidence was strongly compensated by other determinants, deeming a downgrade from high quality of evidence for this outcome unjustified.

3.5.1 | Angular deviation

Significantly greater deviation values were associated with FHIP, in comparison with sCAIP ($p < .00001$, MD = 4.41°, 95% CI 3.99–4.83, $I^2 = 84.0\%$), as shown in Figure 4a. This was also the case considering the second test group described in the study of Schneider et al. (2019) (Schneider et al., 2019) ($p < .00001$, MD = 4.37 °, 95% CI 3.98–4.76, $I^2 = 84.0\%$), as displayed in Figure 4a. Similarly, significantly greater deviation values were associated with PGIP, in comparison with sCAIP ($p < .0001$, MD = 2.11°, 95% CI 1.06–3.16, $I^2 = 84.0\%$), as shown in Figure 5a. This was also the case considering the second test group described in the study of Varga et al. ($p < .00001$, MD = 1.44 o, 95% CI 0.90–1.98, $I^2 = 0\%$), as displayed in Figure 5a (Varga et al., 2020).

3.5.2 | Three-dimensional bodily deviation

As described earlier in this manuscript, 3D bodily deviation is defined as the discrepancy between the planned and actual implant position in the bucco-lingual and/or mesio-distal planes relative to coronal and apical landmarks on the implant body. Thus, in the literature, each of these displacements (coronal and apical) is measured independently and has been treated correspondingly in the quantitative analyses.

Coronal deviation

This category of deviation exhibited a significant degree of difference between sCAIP and FHIP, in favor of sCAIP ($p < .00001$, MD = 0.65 mm, 95% CI 0.50–0.79, $I^2 = 99.0\%$) (Figure 4b), albeit

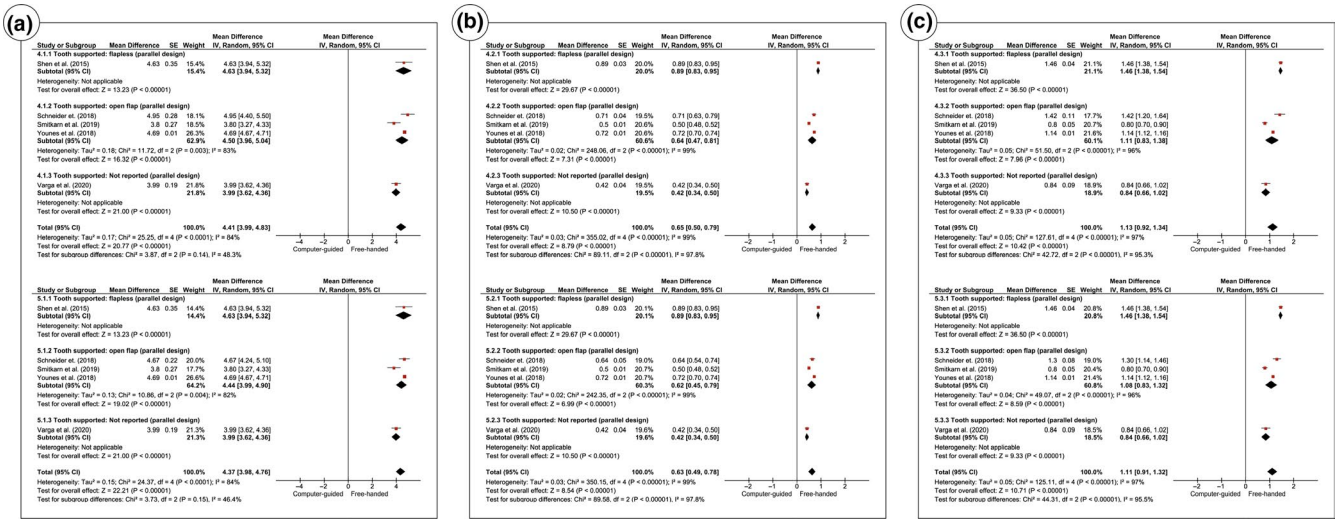

FIGURE 4 Forest plots for (a) angular, (b) coronal, and (c) apical deviation between sCAIP and FHIP considering the (1) first and (2) second test groups included in the study by Schneider et al. (2019), as shown in Table 2

to a much lesser clinical significance than angular and apical deviation. This outcome was comparable with the inclusion of the second test group described in the study by Schneider et al. (Schneider et al., 2019) ($p < .00001$, MD = 0.63 mm, 95% CI 0.49–0.78, $I^2 = 99.0\%$), as depicted in Figure 4b. With respect to both comparisons involving PGIP versus. sCAIP, no statistically significant differences ($p > .05$) between coronal deviation values were identified (Figure 5b).

Apical deviation

Analysis of the evidence on apical deviation showed a significant discrepancy in final implant position between FHIP and sCAIP, in favor of the latter approach ($p < .00001$, MD = 1.13 mm, 95% CI 0.92–1.34, $I^2 = 97.0\%$), as depicted in Figure 4c. Including in the analysis the second test group in the study by Schneider et al. (Schneider et al., 2019), yet again, a similar outcome was observed ($p < .00001$, MD = 1.11 mm, 95% CI 0.91–1.32, $I^2 = 97.0\%$) (Figure 4c). For this parameter, none of the comparisons involving PGIP versus. sCAIP (Figure 5c) showed evidence of significant differences between groups ($p > .05$).

4 | DISCUSSION

4.1 | Summary of main findings

The central aim of this systematic review was to identify and analyze the most relevant evidence pertaining to sCAIP, while exploring new avenues to comprehensively address its clinical applicability, on the basis of a robust PRISMA-compliant methodology.

The final set of included studies amounted to 10 RCTs (Arisan et al., 2010; Farley et al., 2013; Fortin et al., 2006; Magrin et al., 2020; Sancho-Puchades et al., 2019; Schneider et al., 2018, 2019; Shen et al., 2015; Smitkarn et al., 2019; Varga et al., 2020; Vercruyssen, Cox, et al., 2014; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014; Younes et al., 2018). Qualitative data analysis pertaining to the included studies was conducted and, when feasible, the reported data were pooled for the conduction of quantitative analyses.

While implant success rates were not reported by any of the included studies, implant survival rates were reported by 4 of the studies (Arisan et al., 2010; Schneider et al., 2018; Shen et al., 2015; Vercruyssen, van de Wiele, et al., 2014). The demonstrated 2-week to 12-month rates ascribed to sCAIP procedures ranged between 98.02% and 100%, with 100% being the majority finding; in three of the four studies (Schneider et al., 2018; Shen et al., 2015; Vercruyssen, van de Wiele, et al., 2014). All in all, the evidence regarding implant survival rate observed in this review does not favor one of the implant placement modalities over the other.

Unsurprisingly, the accuracy of implant placement has been the most assessed outcome measure of CAIP. Qualitative analyses of the evidence summarized in this review significantly favored sCAIP over FHIP and PGIP. The included studies that used tooth-supported surgical guides were sufficient to perform meta-analyses addressing three domains of deviation (Figures 4 and 5), ultimately demonstrating a significantly lower degree of deviation with sCAIP as compared to FHIP in all domains and PGIP for angular deviation only (Farley et al., 2013; Magrin et al., 2020; Schneider et al., 2019; Shen et al., 2015; Smitkarn et al., 2019; Varga et al., 2020; Younes et al., 2018). One of the studies that used bone- and mucosa-supported guides, but was not eligible for inclusion in the pooled estimates, also assessed accuracy and reported a clear benefit in this regard for sCAIP (Vercruyssen, Cox, et al., 2014). A notable finding of these analyses was the considerable discrepancy in mean difference between the coronal (MD = 0.65 mm; 95% CI: 0.50–0.79) and apical (MD = 1.13 mm, 95% CI 0.92–1.34) deviations for the FHIP versus. sCAIP comparison. Because both of these parameters are comprised of metric

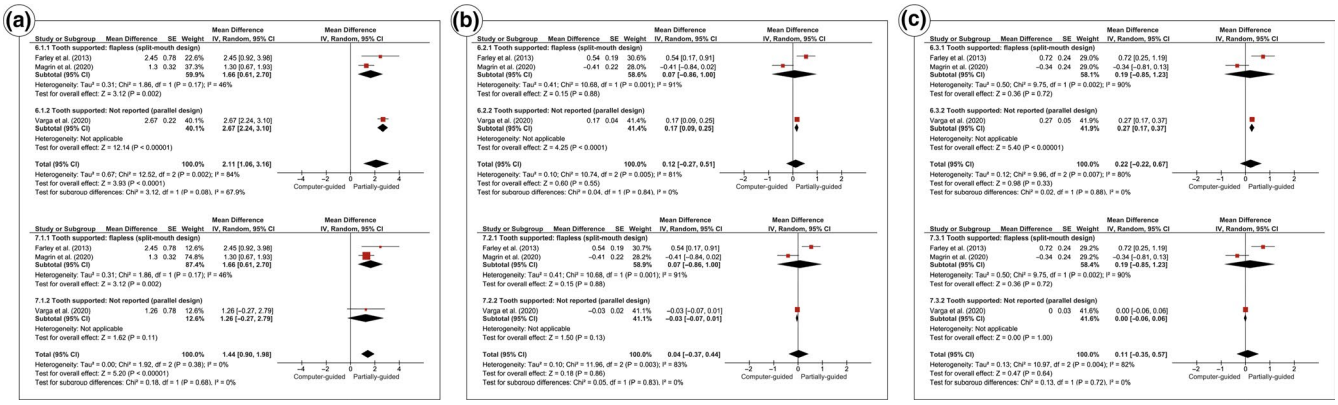

FIGURE 5 Forest plots for (a) angular, (b) coronal, and (c) apical deviation between sCAIP and PGIP considering the (1) first and (2) second test groups included in the study by Varga et al. (2020), as shown in Table 2

measurements in 3D space, this discrepancy can be recognized as the logical, positional outcome of a greater resultant distance between two implant apices and two implant shoulders, when a deviation occurs. While there may be a slight deviation at the entry point between two implants, as the implant is placed deeper into bone, the apices diverge further away from each other. This draws attention to how sCAIP can contribute to control, not only the impact of the deviation at the entry point on the positional adequacy for prosthetic rehabilitation, but also deviation at the implant apex, whereby important anatomical structures may be invaded.

Making the assumption that superior implant survival and accuracy is sufficient to deem sCAIP a beneficial implant placement technique would be painting an incomplete clinical picture. Therefore, it becomes of paramount importance to address other clinical facets associated with sCAIP, such as PROMs. The PROMs provided by the studies included in this review are majorly heterogeneous in nature, although some outcomes were common to all (Tables 2 and 4). Considering that both the bone-supported surgical guide and FHIP groups were coupled with an open flap approach, as opposed to the flapless approach associated with the mucosa-supported surgical guide study group (Table 2), it can be assumed that the discrepancy in postoperative discomfort may be primarily attributed to the degree of invasiveness of the surgical approach.

Broadly speaking, the findings on postoperative pain were split between being comparable among groups (Magrin et al., 2020; Sancho-Puchades et al., 2019; Vercruyssen, De Laat, et al., 2014; Vercruyssen, van de Wiele, et al., 2014), and being significantly lower in cases of flapless, computer-aided placement (Arisan et al., 2010; Fortin et al., 2006). It is important to mention, however, that one of the latter studies had only consisted of study groups undergoing an open flap approach (Sancho-Puchades et al., 2019). This heterogeneity in the nature of the study groups suggests that these findings should be extrapolated with caution.

Other endpoints reported in the selected studies (e.g., procedural duration, cost analysis etc.) were not included in the original set of outcomes of interest and have thus been considered to be outside the scope of this review. However, it must be mentioned that treatment cost may be an important factor influencing operator and patient willingness to pursue sCAIP. Joda et al. (2018) conducted a systematic review addressing this aspect, wherein the results suggested a degree of inconclusiveness due to either data heterogeneity or a lack of evidence (Joda et al., 2018). This aspect should be subject of further research.

4.2 | Quality of the evidence and potential biases in the review process

In an effort to present a valuable update on contemporary evidence regarding CAIP, this systematic review and meta-analysis were based on a rigorous inclusion of studies on the topic. As previously mentioned, earlier systematic reviews often failed to omit study designs that provided minimal to no clinical significance, whereas the final set of included studies in this review were all RCTs. This immediately proposes more rigorous results that may be directly extrapolated to clinical practice. The overall risk of bias was evenly split between low-risk (n = 5) and high-risk (n = 5) studies, where most the common area for risk was in the measurement of the outcome. This domain impacts study quality differently, depending on the outcome measure of interest. For example, PROMs can be influenced by failure to mask outcome assessment (the patient, in this case) because psychological factors may heavily affect perception of such outcomes. This, in addition to inconsistency among trials, played a role in downgrading to low quality for this outcome. On the other hand, this limitation in study design was not considered as critical in the outcome assessment of accuracy due to the different nature of this assessment; blinding being less potentially detrimental to the data. A more homogenous dataset that allowed for generating pooled data analyses may compensate for this, enabling us to comfortably conclude that further research is unlikely to change our confidence in the estimate of effect concerning this outcome measure (high quality). Additionally, publication bias could not be properly evaluated because of the limited number of studies included in the meta-analysis (n = 8). According to the Cochrane Handbook,

"Although funnel plot asymmetry has long been used to detect publication bias, as a rule of thumb, tests for funnel plot asymmetry should be used only when there are at least 10 studies included in the meta-analysis, because when there are fewer studies the power of the tests is low."

4.3 | Agreements and disagreements with other studies or reviews

This systematic review is preceded by a substantial body of literature addressing the applicability of sCAIP, including several meta-analyses. Unfortunately, much of the evidence available in existing systematic reviews has either presented suboptimal study designs, which directly affects the validity of observation, and/or drifted away from research questions of clinical relevance. Nonetheless, a handful of original studies have provided the scientific community with sound data regarding digitally planned and executed implant placement therapy.

The implant survival rate outcomes of this review aligned with the short-term survival rates commonly reported in the recent literature (Pjetursson, Thoma, Jung, Zwahlen, & Zembic, 2012). With comparable values for each modality, this is a corroboration of previous reviews that have reported comparable short-term implant survival rates (Colombo et al., 2017; Laleman et al., 2016; Pozzi et al., 2016; Tahmaseb, Wu, Wismeijer, Coucke, & Evans, 2018).

Accuracy favoring sCAIP over the other modalities has been observed in a very brief number of preceding systematic reviews, most resorting to only assessing deviations within sCAIP due to a previous lack of studies (Bover-Ramos et al., 2018; Colombo et al., 2017; Pozzi et al., 2016; Seo & Juodzbalys, 2018). However, this review distinctly presents solid evidence that allowed for the conduction of the first meta-analysis of data emanating exclusively from comparable RCTs. A recent meta-analysis of all clinical study designs (Tahmaseb et al., 2018) stated that sCAIP deviations remain within a clinically acceptable range, including that, at the very least, a 2-mm margin of error is to be abided by during the position planning phase. A systematic review published in 2018 tenuously concluded that mucosa-supported surgical guides are not, but can be, associated with considerable deviation, depending on bone density, mucosal thickness, surgical technique, smoking habits, and implant length (Seo & Juodzbalys, 2018). The authors shed light on the ranges of expected deviation according to the available literature (0.67–2.19 mm, 0.6–1.68 mm, and 2.6° to 4.67° for apical, coronal, and angular deviation, respectively).

In spite of the positive findings pertaining to the accuracy of sCAIP, the pragmatism of its clinical application may still be questioned. One of the studies included in this review reported that in 19 of the computer-aided cases, an inability to implement the use of the custom-tailored, prefabricated surgical guide warranted deviation from the protocol (Schneider et al., 2019). Although the authors failed to detail the grounds on which such a decision was undertaken, it may raise the question of whether a surgical guide can in fact be used whenever needed. This emphasizes the necessity for ideal case selection and thorough planning throughout the entire diagnostic and treatment planning digital workflow. Interestingly, some studies have sought the most favorable clinical circumstances by investigating the impact of many modifiable and non-modifiable factors on accuracy of placement (Sigcho Lopez et al., 2019; Zhou et al., 2018). In a recent publication, a multiple linear regression model detailing important relationships between factors associated with sCAIP and the deviation of final implant position demonstrated that certain positions in the oral cavity, such as maxillary posterior region, displayed a greater propensity for deviation (Smitkarn et al., 2019). Similarly, a second research group published a series of articles, one of which seems to provide little to no clinical relevance (El Kholy, Ebenezer, et al., 2019), on important treatment planning factors that may also serve as predictors for success (El Kholy, Janner, Schimmel, & Buser, 2019; El Kholy, Lazarin, et al., 2019). The authors pointed to clinical elements, including the number and type of teeth used for a guide's support, surgical guide construct, and total drilling distance below the guide sleeve, that may heavily influence the clinical outcome. The reliability of the reported findings on these factors, in terms of clinical implication, may not be broadly affirmed for sCAIP across the board; however, further research in these areas, particularly with comparable study designs, may yield strong evidence for translation into specific clinical scenarios.

In general, the diversity of reported pain-related outcomes, seen in the outcomes of this review, is not an unprecedented finding in grouped descriptive analyses of the available literature (Colombo et al., 2017; Joda et al., 2018; Laleman et al., 2016). Previous systematic reviews have also pointed toward an expected lesser magnitude of postoperative discomfort associated with sCAIP that may be due to a flapless approach (Colombo et al., 2017; Joda et al., 2018); a claim which is unsubstantiated but may pose empirical merit. In that regard, the available heterogeneity calls for standardized research protocols that isolate specific PROMs associated with sCAIP.

5 | CONCLUSIONS

Based on the finding from this systematic review, it can be concluded that sCAIP provides tangible clinical advantages over conventional (i.e., FHIP and PGIP) implant placement methods across several domains, as long as the clinical situation permits the stabilization of a surgical guide and an unhindered drilling sequence. Quantitative analyses support the superiority of sCAIP over FHIP in all parameters associated with accuracy of placement and over PGIP in angular deviation. Patient perception of treatment in terms of reported intra- or postoperative discomfort seems to be highly dependent on procedural events associated with implant placement (i.e., raising a flap, utilizing guide fixation screws, multiple surgical sites and concomitant ridge augmentation, among others) as opposed to the modality of placement itself. Future research should focus on evaluating key factors (e.g., anatomical and technological)

that may contribute to successful sCAIP via well-designed and properly conducted clinical studies.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

G.A. conceived the idea; M.T. and G.A. screened the initial entries, selected the articles and collected the data; L.C. analyzed the data; O.G. provided expert clinical perspective for the discussion; M.T. and G.A. led the writing; G.A. is the guarantor of the review.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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