CAD/CAM vs Conventional Technique for Fabrication of Implant-Supported Frameworks: A Systematic Review and Meta-Analysis of In Vitro Studies

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Purpose: To compare the marginal vertical misfit between implant-supported frameworks fabricated using CAD/CAM systems and the conventional technique (lost-wax casting). Materials and Methods: This review was performed according to PRISMA criteria and registered on PROSPERO (CRD42017055685). An electronic search was performed independently by two examiners in the MEDLINE (Pubmed), Embase, Web of Science, and Cochrane Library databases to find studies published up to April 2018. *Results:* The database search yielded 507 references. After removing duplicate references, 384 studies remained. Eleven in vitro studies were selected according to the eligibility criteria (inter-reader κ = 0.88). Nine different CAD/CAM systems were used to fabricate 172 frameworks of different materials, including zirconia, monolithic lithium disilicate, and metallic alloys. Subgroup analyses were performed for different types and retention systems of the frameworks. In the general analysis, marginal misfit observed with the CAD/CAM systems was lower than with the conventional method (P = .003), as was observed in the subgroup analysis for single-unit frameworks (P < .00001). For fixed (P = .89), cemented (P = .60), and screwed (P = .18) frameworks, no significant difference was observed between the evaluated techniques. *Conclusion:* The CAD/CAM systems showed improved marginal fit over the conventional lost-wax casting technique for fabricating single-unit frameworks; however, in the subgroup analyses, no difference was observed for the fixed implant-supported type or for the retention systems evaluated. Int J Prosthodont 2019;32:182–192. doi: 10.11607/ijp.5616

A high success rate has been reported for implant-supported prostheses in the literature.^{1,2} The success is directly related to the uniform distribution of stress among all prosthetic components, the properties of the materials used, the technique used to make the frameworks and abutments,³ and the passive fit between the implants and abutments.⁴

Given the difficulty in achieving complete/total fit of the implants and the frameworks, some authors have accepted that well-controlled manufacturing techniques are capable of providing a long-term successful implant treatment. Based on this reasoning and on the literature, the fit condition is generally understood as a passive fit condition, defined as the simultaneous and even contact of all fitting surfaces without the development of strains prior to functional loading. On the other hand, based on the concepts used by Jemt et al⁵ (1991), a poor fit or misfit condition is understood when there is a gap opening between the framework and the implant.⁶⁻⁸

The conventional technique is related to the use of metal alloys to make the frameworks, and with its many laboratory steps, these procedures can be related to higher values of misfit.^{9,10} Since the advent of computer-aided design/computer-assisted manufacturing (CAD/CAM) systems, which necessitate fewer clinical steps and shorter time to conclude the rehabilitation treatment, studies report greater accuracy and fit for frameworks and abutments when compared to the conventional technique.^{11,12}

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Submitted August 3, 2017; accepted October 4, 2018. ©2019 by Quintessence Publishing Co Inc. CAD/CAM also introduced the use of different materials for confection of the frameworks.^{3,13–15}

Some studies^{16–18} highlight that the presence of poor fit or misfit, whether clinically detectable or not, can induce internal stresses in the framework, the implants, and the bone surrounding the implants¹⁵ and may even originate a bacterial colonization inducing biologic^{8,19–21} and mechanical complications, such as loosening of the screws, crown debonding, and/or fracture of abutments, frameworks, and prosthetic crowns.^{22,23}

Clinical studies comparing the two manufacturing techniques are scarce in the literature. There is no consensus about the superiority of CAD/CAM compared to the conventional technique. Some in vitro studies found that the conventional method was more favorable than CAD/CAM,²⁴ while others observed a statistical similarity between the two techniques,²⁵ and still others reported lower misfit values compared to the CAD/CAM technique.³

For this reason, the aim of this systematic review was to evaluate the marginal misfit (gap in the margin external or internal to the implant-framework interface) of implant-supported frameworks fabricated using CAD/ CAM systems and the conventional method (lost-wax casting technique). The null hypothesis was the following: Frameworks fabricated using CAD/CAM technology and those fabricated using the conventional technique would show no difference in marginal vertical misfit values.

MATERIALS AND METHODS

Protocol and Registration

This systematic review with meta-analysis was structured based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)²⁶ and according to other models proposed in the literature.^{27,28} Moreover, this study was recorded on the PROSPERO registration platform (CRD42017055685).

Eligibility Criteria

The eligibility criteria for selection of the studies were: randomized controlled trials (RCT); prospective studies (cohort studies); retrospective studies; case series; in vitro studies; and studies that involved fabrication of implant-supported frameworks using the lost-wax casting technique as the control group. The exclusion criteria were: duplicate studies; systematic reviews; and studies presenting only groups involving CAD/CAM systems or only groups involving fabrication of the frameworks using the lost-wax casting technique without a comparative analysis.

The PICO (population, intervention, comparison, outcome) question was: Are CAD/CAM systems more accurate for fabrication of implant-supported frameworks than the conventional method of lost-wax casting with respect to marginal misfit? According to these criteria, the population was implant-supported frameworks; the intervention was manufactured using CAD/CAM (scanning + design + milling); the comparison was the conventional method (lost-wax casting technique); and the outcome was the marginal vertical misfit.

Information Sources and Search Strategy

Two independent examiners (C.C.M. and C.A.A.L.) conducted an electronic search of MEDLINE (PubMed), Embase, Web of Science, and the Cochrane Library for articles published up to April 2018. The following search terms were used: (((Dental implant [All Fields] OR Dental implants [MeSH Terms])) AND (Computer-Aided Design [MeSH Terms] OR COmputer-Aided Manufacturing [MeSH Terms] OR CAD-CAM [All Fields])) AND (Marginal fit [All Fields] OR Fit [All Fields] OR Misfit [All Fields] OR Marginal misfit [All Fields]).

The same examiners performed a hand search with the same terms for articles published up to March 2018 in the International Journal of Prosthodontics, Journal of Prosthetic Dentistry, Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, International Journal of Oral and Maxillofacial Implants, International Journal of Oral and Maxillofacial Surgery, Journal of Oral and Maxillofacial Surgery, Journal of Clinical Periodontology, Journal of Dental Research, Journal of Oral Implantology, Journal of Oral Rehabilitation, Journal of Periodontology, Periodontology 2000, International Journal of Periodontics and Restorative Dentistry, European Journal of Esthetic Dentistry, and Journal of Prosthodontics. All differences in choices between the examiners were analyzed by a third examiner (E.P.P.), and consensus was reached through discussion.

Data Collection Process

The data extracted from the articles were sorted as quantitative or qualitative by one of the researchers (C.A.A.L) and then checked by another researcher (J.M.L.G.). Any disagreements were resolved through discussion until consensus was reached.

Summary Measures

The meta-analysis was based on the inverse variance method due to the continuous outcome measures, which were reported as mean difference (MD) with 95% confidence intervals (CI). In order to evaluate the manufacturing methods, a quantitative analysis comparing the marginal misfit values (μ m) of CAD/CAM systems to the lost-wax casting technique was performed. Additionally, there was a subgroup analysis for single-unit, fixed, cemented, and screw-retained frameworks. The MD values were considered significant when P < .05. The I² statistic was used to express the percentage of the total variation across studies due to heterogeneity, and I² values above 75% (range 0 to 100) were

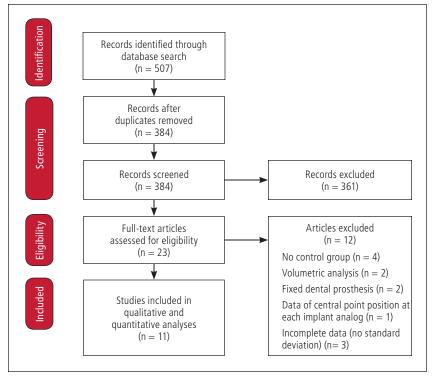


Fig 1 Flowchart showing the procedure for study selection.

considered high and to indicate significant heterogeneity.^{29,30} In case of statistically significant (P < .10) heterogeneity, a random-effects model was used to assess the significance of treatment effects. Where no statistically significant heterogeneity was found, analysis was performed using a fixed-effects model.^{31,32} Review Manager (RevMan v5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for the meta-analysis and to create the forest plots. The kappa coefficient was calculated to determine the inter-reader agreement in the study selection process.

Quality Assessment of Included Studies

A quality assessment of eligible studies was performed using the Critical Appraisal Skills Program (CASP)³³ and MINORS (Methodological Index for Non-Randomized Studies).³⁴ The CASP tool uses a systematic approach based on the following 12 specific criteria:

- 1. The study issue is clearly focused.
- 2. The cohort is recruited in an acceptable way.
- 3. The exposure is accurately measured.
- 4. The outcome is accurately measured.
- 5. Confounding factors are addressed.
- 6. The follow-up is long and complete.
- 7. The results are clear.
- 8. The results are precise.
- 9. The results are credible.
- 10. The results can be applied to the local population.
- 11. The results fit with the available evidence.
- 12. There are important clinical implications.

Each criterion received a response of "yes," "no," or "cannot tell." Each study could have a maximum score of 12. CASP scores were used to grade

the methodologic quality of each study assessed.^{33,35}

Similar to the original MINORS scale,³⁴ the adapted scale consists of 10 items, with 2 additional items proposed for in vivo studies. Each item is scored from 0 to 2; for most items, 0 indicates that the content of the item is not reported, 1 indicates that the content is reported but inadequately, and 2 indicates that it is sufficiently reported. Discrepancies between the two reviewers were discussed until both came to an agreement, and the final score was calculated. The maximum possible score for the in vitro studies was 20 and for in vivo was 24.34

RESULTS

Literature Search

The details of the search strategy are illustrated in Fig 1. Through the searches in the selected databases. 507 articles were found (PubMed/ Medline: 187; Web of science: 157; Embase: 158; and Cochrane: 5). After removal of the duplicates, 384 studies remained, of which 361 were excluded and 23 selected for detailed reading of the full text and application of the inclusion and exclusion criteria. All excluded studies and reasons for exclusion are described in Appendix I. Eleven studies published between 2011 and 2018 were selected for data extraction and qualitative and quantitative analyses.^{12,24,36-44} However, owing to the absence of clinical studies evaluating prosthetic marginal misfit, and especially the absence of studies comparing the two techniques selected, all selected studies were in vitro studies. The inter-reader test performed to obtain the kappa concordance values revealed a high concordance (almost perfect) index in the search stages ($\kappa = 0.88$).⁴⁵

Details of the Included Studies

All study characteristics are described in Table 1. For the 11 selected studies, 296 specimens (range 4 to 20 per group) were analyzed

Table 1	Characteristics of Included Studies (n = 11)
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	Sample			No. of implants/ retention	Connection/	Marginal vertica mean (
Study	size (n)	CAD/CAM system	Materials	system	type	CAD/CAM	Control
Karatasli et al ⁴²	10	Lava and DCS	CAD/CAM: Zirconium (3M ESPE/DCS Dental AG)	1/C	IC/SI	LAVA: 24.6 (14.0)	120.1 (33.1)
			Control: Metal alloy (62% Ni, 25% Cr, 9.5% Mo, 3.5% Si)			DCS: 110.1 (36.5)	
Prasad and Al-Kheraif ³⁹	10	Everest Scan Pro 4102 (KaVo)	CAD/CAM: ZS blank, ZH blank, G blank, T blank	1/C	IC/SI	ZS blank: 58.60 (4.40)	91.50 (14.72)
			Control: NiCr alloy (I-Bond 02, Interdent)			ZH blank: 67.71 (5.36) G blank: 54.75 (9.39)	
						T blank: 18.32 (3.42)	
Zaghloul and Younis ⁴¹	10	Cerec 3 (Sirona Dental Systems)	CAD/CAM: Y-TZP (Vita yz) Control: NiCr alloy (Protechno N, Protechno)	2/C	IC/FPD	84.58 (3.767)	42.27 (3.766)
de Araújo et al ⁴⁰	4	Neoshape (Neodent)	CAD/CAM: Zircad and CoCrcad (Neoshape, Neodent) Control: CoCr alloy (Nobilium "PM"; Nobilium American Gold)	3/S	EC/FPD	Zircad: 103.81 (43.15) CoCrcad: 48.76 (13.45)	187.55 (103.63)
Bayramoglu et al ²⁴	20	Cerec Bluecam + Cerec MC XL (Sirona Dental Systems)	CAD/CAM: IPS ZirCAD, (Ivoclar Vivadent) Control: NiCr alloy	2/C	IC/FPD	Zir: 109.3 (46.4)	MCR: 89.6 (23.4) POM: 85.6 (24.3)
de França et al ³⁷ (2015)	4	3Shape D-700 + 3Shape Dental System 2012 (3Shape A/S)	CAD/CAM: Zirconia Neoshape; Neodent CoCrCAD: Co-Cr Neoshape; Neodent	3/S	EC/FPD	ZirCAD: 5.9 (3.6) CoCrCAD: 1.2 (2.2)	CoCrUCci: 11.8 (9.8) CoCrUCcl: 12.9 (11.0)
			Control: CoCrUCcl (castable abutments); CoCr alloy (Nobil Star Ultra; Nobilium)				
de França et al ³⁶ (2017)	4	3Shape D-700 + 3Shape Dental System 2012 (3Shape A/S)	CADZir: Zirconia, Neoshape, Neodent CADCoCR: Cobalt-Chromium, Neoshape, Neodent	3/S	EC/FPD	CADZirc: 5.9 (3.6) CADCoCR: 1.2 (2.2)	11.8 (9.8)
			CASTCoCR: Talladium Microfine, Talladium				
Nejatidanesh et al ³⁸	10	3D Bluecam (Sirona Dental Systems); Optical laser;	CAD/CAM: Zirconium e.Max CAD: IPS e.max CAD LT	1/C	IC/SI	e.MaxCAD: 32.02 (10.38)	59.19 (17.81)
		Cercon eye + Cercon Brain, Degudent	(Ivoclar Vivadent) Cercon: Cercon Base + Cercon Ceram (Degudent)			Cercon: 34.26 (11.41)	
Presotto et al ¹²	10	Ceramill Map 300 scanner + Ceramill	CAD/CAM: CoCr block (AmannGirrbach)	2/S	EC/FPD	41.6 (18.7)	41.6 (28.2)
		Motion 2 (Amann Girrbach)	Control: CoCr alloy (Starloy C; DeguDent Dentsply)				
Pasalı et al ⁴³	10	7 Series (Dental Wings) + DWOS CAD (Dental Wings) + HSC 20 (Linear; DMG Mori)/ inEos X5 (Dentsply Sirona) + inLab SW 4.2.1 (Dentsply Sirona) + inLab MC XL (Dentsply Sirona)	CrCo sintered (M) and presintered block (MS) (CopraBond K; Whitepeaks Dental Solutions + inCoris CC; Dentsply Sirona)	1/S	IC/SI	M: 81 (2) MS: 99 (2)	92 (2)
Moris et al ⁴⁴	8	Ceramill Map 300 (Amann Girrbach)	CAD/CAM: CoCr alloy (Fit Cast Cobalto; Talmax) Control: CoCr alloy (Ceramill	1/S	EC/SI	6.89 (7.44)	4.55 (4.36)
			Sintron; Amann Girrbach)			implant-supported	

NR = not related; Ni = nickel; Cr = chromium; Mo = molybdenum; Si = silicon; S = screwed; C = cemented; SI = single-unit implant-supported crown; FPD = fixed partial denture crowns; IC = internal connection; EC = external connection; Y-TZP = yttrium-stabilized tetragonal zirconia polycrystal; ZS blank = KaVO Everest partially sintered, yttrium-stabilized zirconium oxide; ZH blank = KaVO Everest fully sintered, pressed, yttrium-stabilized zirconium oxide; G blank = KaVo Everest leucite-reinforced glass-ceramic; T blank = KaVo Everest medical pure titanium; MCR = conventional metal-ceramic restorations; POM = press-on-metal restorations.

technique). Nine different CAD/CAM systems, including

(172 fabricated using CAD/CAM and 124 using lost-wax both intraoral and extraoral scanning systems (Lava, DCS, Everest, Cerec Bluecam, Neoshape, 3shape D700,

Study	Alloy	Classification system for alloys ^a
Karatasli et al ⁴²	Ni-Cr-Mo (Mealloy, Dentsply MEA&CIS Division)	Non-noble metal alloy
Prasad and Al-Kheraif ³⁹	Ni-Cr (I-Bond 02, Interdent)	Non-noble metal alloy
Zaghloul and Younis ⁴¹	Ni-Cr (Protechno-N Protechno)	Non-noble metal alloy
de Araújo et al ⁴⁰	Co-Cr-Mo (Nobilium "PM"; Nobilium American Gold; composition: 64% Co, 28.5% Cr, and 5.25% Mo)	Non-noble metal alloy
Bayramoglu et al ²⁴	Ni-Cr alloy	Non-noble metal alloy
de França et al ³⁷ (2015)	Co-Cr (Nobil Star Ultra; Nobilium)	Non-noble metal alloy
de França et al ³⁶ (2017)	Co-Cr (Nobil Star Ultra; Nobilium)	Non-noble metal alloy
Nejatidanesh et al ³⁸	Ni-Cr (Wirocer Plus; Bego)	Non-noble metal alloy
Presotto et al ¹²	Co-Cr (Starloy C; DeguDent Dentsply)	Non-noble metal alloy
Pasali et al ⁴³	Co-Cr (61.1% Co, 27.8% Cr, 8.5% W, 1.7% Si, < 0.5% Mn) (Microlit isi; Schütz Dental)	Non-noble metal alloy
Moris et al ⁴⁴	Co-Cr (Fit Cast Cobalto; Talmax)	Non-noble metal alloy

^ahttps://www.ada.org/en/about-the-ada/ada-positions-policies-and-statements/revised-classification-system-for-alloys-for-fixed-prosthodontics. Ni = nickel; Cr = chromium; Mo = molybdenum; Co = cobalt; W = tungsten; Si = silicon; Mn = manganese.

Table 3	CASP Quality	Assess	ment o	f Incluc	led Stu	dies	
Study		0.1	0.2	03	0.4	05	06

Study	Q 1	Q 2	Q 3	Q 4	Q 5	Q 6	Q 7	Q 8	Q 9	Q 10	Q 11	Q 12	Total
Karatasli et al ⁴²	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Prasad and Al-Kheraif ³⁹	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Zaghloul and Younis ⁴¹	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
de Araújo et al ⁴⁰	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Bayramoglu et al ²⁴	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
de França et al ³⁷ (2015)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
de França et al ³⁶ (2017)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Nejatidanesh et al ³⁸	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Presotto et al ¹²	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Pasali et al ⁴³	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Moris et al ⁴⁴	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	No	Yes	Yes	8

Ceramill Map 300, 7 Series, and inEos X5), were used. Regarding the type of prostheses, the studies evaluated single unit, fixed implant supported, and complete arch. For the materials used for CAD/CAM groups, one group in the eligible studies fabricated leucite-reinforced glassceramic frameworks, another study fabricated monolithic lithium disilicate frameworks, and another group titanium frameworks. Ten groups fabricated zirconium frameworks, and seven fabricated frameworks using different cobalt-chromium alloys. All the included studies used non-noble metal alloys: cobalt-chromium (CoCr),^{12,36,37,43,44} nichrome (NiCr),^{24,38,39,41} NiCrMo,⁴² and CoCrMo⁴⁰ (Table 2).

Six studies^{12,36,37,40,43,44} used screw retention, and five studies^{24,38,39,41,42} used cement retention. Regarding the implant-abutment connection type, six studies^{24,38,39,41–43} used internal connection, and five^{12,36,37,40,44} used external connection.

Quality Assessment of Included Studies

The quality assessment of the individual studies is summarized in Table 3 (CASP) and Table 4 (MINORS). According to the CASP scale, the eligible studies (in vitro) received a "no" rating for criteria 5, 6, and 10. These three negative answers resulted in a total score of 9 for 10 studies and 8 for the last study. For the MINORS scale, all studies showed scores above 16, indicating lower risk of bias.

Meta-analysis

For the quantitative analysis, all 11 studies provided the complete marginal misfit values (with standard deviation [SD]) by comparing the CAD/CAM systems with the lost-wax casting technique. Comparing these values, the difference was statistically favorable for the CAD/CAM group (P = .003; MD –16.06 [CI –26.69 to –5.44]; $I^2 = 99\%$, P < .00001) (Fig 2).

Table 4 Modified Methodologic Index for Nonrandomized Studies (MINORS)

Evaluation	Karatasli et al ⁴²	Prasad and Al-Kheraif ³⁹	Zaghloul and Younis ⁴¹	de Araújo et al ⁴⁰	Bayramoglu et al ²⁴	de França et al ³⁷ (2015)	de França et al ³⁶ (2017)	Nejatidanesh et al ³⁸	Presotto et al ¹²	Pasali et al ⁴³	Moris et al ⁴⁴
Clearly stated aim	2	2	2	2	2	2	2	2	2	2	2
Contemporary groups	2	2	2	2	2	2	2	2	2	2	2
Prospective collection of data	2	2	2	2	2	2	2	2	2	2	2
Sample randomization	0	0	0	0	0	0	1	0	0	0	0
Test group milling material: (0 [not reported], 1 [presintered/crystallized material], 2 [final phase, sintered, monolithic material or metallic material])	1	1	0	1	1	1	1	1	1	1	2
Measurement standardization	2	2	2	1	1	1	1	0	1	1	2
Condition of the samples during measurements	0	2	0	2	2	2	2	2	2	2	2
Measurement method	2	2	2	2	1	2	2	2	2	2	2
Endpoints appropriate to the aim of the study	2	2	2	2	2	2	2	2	2	2	2
Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	2	0	0
Prospective calculation of the study size	0	0	0	0	2	0	0	0	0	2	0
Baseline equivalence of groups	2	2	2	2	2	2	2	2	2	2	2
Adequate statistical analyses	2	2	2	2	2	2	2	2	2	2	2
Total Score	17	19	16	18	19	18	19	17	20	20	20

0 = not reported; 1 = reported but inadequately; 2 = reported and adequate.

The global ideal score is 16 for noncomparative studies and 24 for comparative studies.

	CAD/CA	M	Contol		Weight	Mean difference	Mean o	lifference
Study	Mean, SD	Total	Mean, SD	Total	(%)	IV, random, 95% CI	IV, rando	m, 95% CI
de Araújo et al (CoCrcad) ⁴⁰	48.76, 13.45	4	187.55, 103.63	4	0.9	-138.79 (-241.20, -36.38)	~	
de Araújo et al (Zircad) ⁴⁰	103.81, 43.15	4	187.55, 103.63	4	0.8	-83.74 (-193.75, 26.27)	\leftarrow	+
Pasali et al (M) ⁴³	81, 2	10	92, 2	10	5.7	–11.00 (–12.75, –9.25)	1	r
Pasali et al (MS) ⁴³	99, 2	10	92, 2	19	5.7	7.00 (5.47, 8.53)		-
Bayramoglu et al (MCR) ²⁴	109.3, 46.4	20	89.6, 23.4	20	4.5	19.70 (-3.07, 42.47)		├- ∎
Bayramoglu et al (POM) ²⁴	109.3, 46.4	20	85.6, 24.3	20	4.5	23.70 (0.74, 46.66)		
de França et al (CADCoCr) ³⁶	1.2, 2.2	4	11.8, 9.8	4	5.4	-10.60 (-20.44, -0.76)	-	r-
de França et al (CADZirc) ³⁶	5.9, 3.6	4	11.8, 9.8	4	5.4	–5.90 (–16.13, 4.33)	-	╺┼
de França et al (CoCrCAD) ³	1.2, 2.2	4	12.9, 11	4	5.4	–11.70 (–22.69, –0.71)	-	
de França et al (ZirCAD) ³	5.9, 3.6	4	12.9, 11	4	5.3	-7.00 (-18.34, 4.34)	-	∎┼
Karatasli et al (DCS) ⁴²	110.1, 36.5	10	120.1, 33.1	10	3.9	-10.00 (-40.54, 20.54)		- +
Karatasli et al (LAVA) ⁴²	24.6, 14	10	120.1, 33.1	10	4.5	–95.50 (–117.77, –73.23)		
Moris et al ⁴⁴	6.89, 7.44	8	4.55, 4.36	8	5.6	2.34 (-3.64, 8.32)		+
Nejatidanesh et al (Cercon) ³⁸	34.26, 11.41	10	59.19, 17.81	10	5.2	-24.93 (-38.04, -11.82)		
Nejatidinesh et al (e.MaxCAD) ³⁸	32.02, 10.38	10	59.19, 17.81	10	5.3	–27.17 (–39.95, –14.39)		
Prasad and Al-Kheraif (G blank) ³⁹	54.75, 9.39	10	91.5, 14.72	10	5.4	–36.75 (–47.57, –25.93)		
Prasad and Al-Kheraif (T blank) ³⁹	18.32, 3.42	10	91.5, 14.72	10	5.4	-73.18 (-82.55, -63.81)		
Prasad and Al-Kheraif (ZH blank) ³⁹	67.71, 5.36	10	91.5, 14.72	10	5.4	-23.79 (-33.50, -14.08)		
Prasad and Al-Kheraif (ZS blank) ³⁹	58.6, 4.4	10	91.5, 14.72	10	5.4	-32.90 (-42.42, -23.38)	-	
Presotto et al ¹²	41.6, 18.7	10	41.6, 28.2	10	4.7	0.00 (-20.97, 20.97)	-	↓
Zaghloul and Younis ⁴¹	84.58, 3.767	10	42.27, 3.766	10	5.7	42.31 (39.01, 45.61)		
Total (95% CI)		192		201	100.0	–16.06 (–26.69, –5.44)	•	
Heterogeneity: Tau ² = 517.17; χ^2 =	= 1,338.16; df =	20 (P <	< .00001); l ² = 99	9%.				
Test for overall effect: $z = 2.96$, $P =$.003						 10050	1 I I 0 50 100
							Favors (CAD/CAM)	Favors (Control

Fig 2 Forest plot for overall marginal misfit values (μ m). The overall effect estimate was favorable for frameworks fabricated with CAD/CAM systems when compared to the lost-wax casting technique (P = .003).

	CAD/CA	M	Contol		Weight	Mean difference		Mean diff	erence	
Study	Mean, SD	Total	Mean, SD	Total	(%)	IV, random, 95% CI		IV, random,	95% CI	
Pasali et al (M) ⁴³	81, 2	10	92, 2	10	10.2	–11.00 (–12.75, –9.25)		T		
Pasali et al (MS) ⁴³	99, 2	10	92, 2	10	10.2	7.00 (5.25, 8.75)			Ŧ	
Karatasli et al (DCS) ⁴²	110.1, 36.5	10	120.1, 33.1	10	6.0	-10.00 (-40.54, 20.54)				
Karatasli et al (LAVA) ⁴²	24.6, 14	10	120.1, 33.1	10	7.4	–95.50 (–117.77, –73.23)	←			
Moris et al ⁴⁴	6.89, 7.44	8	4.55, 4.36	8	10.0	2.34 (-3,64, 8.32)		-	-	
Nejatidanesh et al (Cercon) ³⁸	34.26, 11.41	10	59.19, 17.81	10	9.0	-24.93 (-38.04, -11.82)		_		
Nejatidinesh et al (e.MaxCAD) ³⁸	32.02, 10.38	10	59.19, 17.81	10	9.1	–27.17 (–39.95, –14.39)		_		
Prasad and Al-Kheraif (G blank) ³⁹	54.75, 9.39	10	91.5, 14.72	10	9.4	–36.75 (–47.57, –25.93)				
Prasad and Al-Kheraif (T blank) ³⁹	18.32, 3.42	10	91.5, 14.72	10	9.6	–73.18 (–82.55, –63.81)				
Prasad and Al-Kheraif (ZH blank) ³⁹	67.71, 5.36	10	91.5, 14.72	10	9.5	-23.79 (-33.50, -14.08)				
Prasad and Al-Kheraif (ZS blank) ³⁹	58.6, 4.4	10	91.5, 14.72	10	9.6	-32.90 (-42.42, -23.38)		-		
Total (95% CI)		108		108	100.0	-28.48 (-40.10, -16.86)		•		
Heterogeneity: Tau ² = 343.79; χ^2 =	598.60; df = 2	0 (P < .0	00001); l ² = 989	%.						
Test for overall effect: $z = 4.80$, $P <$.00001						-100	-50 () 50) 100
							Favors CA	D/CAM	Fav	ors control

Fig 3 Forest plot for single-unit framework marginal misfit values (μ m). The overall effect estimate was favorable for frameworks fabricated using CAD/CAM systems when compared to the lost-wax casting technique (P < .00001).

Study	CAD/CA		Contol	Tatal	Weight	Mean difference		Mean diff		
	Mean, SD	Total	Mean, SD	Total	(%)	IV, random, 95% CI		IV, random,	95% CI	
de Araújo et al (CoCrcad) ⁴⁰	48.76, 13.45	4	187.55, 103.63	4	3.4	-138.79 (-241.20, -36.38)	\leftarrow	_		
de Araújo et al (Zircad) ⁴⁰	103.81, 43.15	4	187.55, 103.63	4	3.1	-83.74 (-193.75, 26.27)	\leftarrow			
Bayramoglu et al (MCR) ²⁴	109.3, 46.4	20	89.6, 23.4	20	11.0	19.70 (-3.07, 42.47)		ł		
Bayramoglu et al (POM) ²⁴	109.3, 46.4	20	85.6, 24.3	20	10.9	23.70 (0.74, 46.66)		-		
de França et al (CADCoCr) ³⁶	1.2, 2.2	4	11.8, 9.8	4	12.1	-10.60 (-20.44, -0.76)				
de França et al (CADZirc) ³⁶	5.9, 3.6	4	11.8, 9.8	4	12.1	-5.90 (-16.13, 4.33)				
de França et al (CoCrCAD) ³	1.2, 2.2	4	12.9, 11	4	12.0	-11.70 (-22.69, -0.71)				
de França et al (ZirCAD) ³	5.9, 3.6	4	12.9, 11	4	12.0	-7.00 (-18.34, 4.34)				
Presotto et al ¹²	41.6, 18.7	10	41.6, 28.2	10	11.1	0.00 (-20.97, 20.97)		-+		
Zaghloul and Younis ⁴¹	84.58, 3.767	10	42.27, 3.766	10	12.3	42.31 (39.01, 45.61)				
Total (95% CI)		84		84	100.0	–1.55 (–23.72, 20.63)				
Heterogeneity: Tau ² = 1,033.77;	$\chi^2 = 281.31; df =$	9 (P <	.00001); l ² = 979	6.						
Test for overall effect: $z = 0.14$, P	= .89						-100 -	-50 0	50	100
							Favors CAD/			s control

Fig 4 Forest plot for fixed partial denture marginal misfit values (μ m). The overall effect estimate was not significant between the manufacturing methods analyzed (P = .89).

In a subgroup analysis for each type of framework fabricated in the selected studies, a significant favorable difference was observed for single-unit frameworks fabricated using CAD/CAM systems in comparison to the control group (P < .00001; MD –28.48 [CI –40.10 to –16.85]; I² = 98%, P < .00001) (Fig 3). Implant-supported fixed partial frameworks were evaluated in six studies, and no significant difference was observed in the comparison between CAD/CAM and the conventional method (P = .89; MD –1.55 [CI –23.72 to 20.63]; I² = 97%, P < .00001) (Fig 4).

Different retention systems (cemented and/or screwed) were used and evaluated in the studies. In the subgroup analysis of both retention systems, no significant difference was observed between the marginal misfit values when comparing CAD/CAM to the conventional method (cemented: P = .60, MD -10.07 [CI -47.68 to 27.54]; I² = 98%, P < .00001; Fig 5; screwed: P = .13, MD -5.91 [CI -14.51 to 2.68]; I² = 96%, P < .00001; Fig 6).



	CAD/CA	M	Contol		Weight	Mean difference		Mean	differen	ice	
Study	Mean, SD	Total	Mean, SD	Total	(%)	IV, random, 95% CI		IV, rand	om, 959	% CI	
Bayramoglu et al (MCR) ²⁴	109.3, 46.4	20	89.6, 23.4	20	14.1	19.70 (-3.07, 42.47)					
Bayramoglu et al (POM) ²⁴	109.3, 46.4	20	85.6, 24.3	20	14.1	23.70 (0.74, 46.66)			-	•	
Karatasli et al (DCS) ⁴²	110.1, 36.5	10	120.1, 33.1	10	13.5	-10.00 (-40.54, 20.52)					
Karatasli et al (LAVA) ⁴²	24.6, 14	10	120.1, 33.1	10	14.1	–95.50 (–117.77, –73.23)	←				
Nejatidanesh et al (Cercon) ³⁸	34.26, 11.41	10	59.19, 17.81	10	14.6	-24.93 (-38.04, -11.82)			-		
Nejatidinesh et al (e.MaxCAD) ³⁸	32.02, 10.38	10	59.19, 17.81	10	14.6	–27.17 (–39.95, –14.39)		_	-		
Zaghloul and Younis ⁴¹	84.58, 3.767	10	42.27, 3.766	10	14.9	42.31 (39.01, 45.61)				•	
Total (95% Cl)		90		90	100.0	–10.07 (–47.68, 27.54)				•	
Heterogeneity: Tau ² = 2,474.72; χ	² = 326.77; df =	6 (P<.	.00001); I ² = 98	%.							
Test for overall effect: $z = 0.52$, $P =$	= .60						-100	-50	0	50	100
							Favors CA	AD/CAM		Favors	control

Fig 5 Forest plot for cement-retained framework marginal misfit values (μ m). The overall effect estimate was not significant between the manufacturing methods analyzed (P = .60).

	CAD/CA	M	Contol		Weight	Mean difference		Mean	differen	ce	
Study	Mean, SD	Total	Mean, SD	Total	(%)	IV, random, 95% CI		IV, rando	om, 95%	6 CI	
de Araújo et al (CoCrcad) ⁴⁰	48.76, 13.45	4	187.55, 103.63	4	0.7	-138.79 (-241.20, -36.38)	\leftarrow				
de Araújo et al (Zircad) ⁴⁰	103.81, 43.15	4	187.55, 103.63	4	0.6	-83.74 (-193.75, 26.27)	\leftarrow		_		
Pasali et al (M) ⁴³	81, 2	10	92, 2	10	14.6	–11.00 (–12.75, –9.25)		-			
Pasali et al (MS) ⁴³	99, 2	10	92, 2	10	14.6	7.00 (5.25, 8.75)			-		
de França et al (CADCoCr) ³⁶	1.2, 2.2	4	11.8, 9.8	4	12.3	-10.60 (-20.44, -0.76)			_		
de França et al (CADZirc) ³⁶	5.9, 3.6	4	11.8, 9.8	4	12.2	–5.90 (–16.13, 4.33)			┏┼╴		
de França et al (CoCrCAD) ³	1.2, 2.2	4	12.9, 11	4	11.8	–11.70 (–22.69, –0.71)			_		
de França et al (ZirCAD) ³	5.9, 3.6	4	12.9, 11	4	11.7	-7.00 (-18.34, 4.34)					
Moris et al ⁴⁴	6.89, 7.44	8	4.55, 4.36	8	13.7	2.34 (-3.64, 8.32)			+		
Presotto et al ¹²	41.6, 18.7	10	41.6, 28.2	10	7.8	0.00 (-20.97, 20.97)			+		
Total (95% Cl)		62		62	100.0	–5.91 (–14.51, 2.68)					
Heterogeneity: Tau ² = 131.08; χ^2	² = 220.66; df = 9	(P < .0	0001); I ² = 96%.								
Test for overall effect: $z = 1.35$, P	°=.18						-50	-25	0	25	50
							Favors CA	D/CAM		Favors	control

Fig 6 Forest plot for screw-retained framework marginal misfit values (μ m). The overall effect estimate was not significant between the manufacturing methods analyzed (P = .18).

DISCUSSION

The purpose of this study was to verify if the literature presents scientific evidence capable of demonstrating the superiority of CAD/CAM systems compared to conventional methods for the fabrication of implantsupported frameworks. From the selected studies and based on the present statistical analyses, it was observed that the first null hypothesis formulated in this study was rejected, since according to general analysis in the in vitro studies the CAD/CAM systems were more accurate and had marginal misfit values significantly lower than those of the frameworks made by the conventional method. Although two in vitro studies^{24,41} observed lower values of misfit for the conventional method, the results found in the present meta-analysis corroborate with the literature that has verified extremely positive results for CAD/CAM systems, not only for producing implant-supported restorations and frameworks but also for manufacturing surgical guides, orthodontic planning, and even complete dentures and removable partial dentures.^{36,38,46,47}

In the individualized subgroup analysis for single-unit restorations, a superior accuracy of CAD/CAM systems was observed compared to the conventional method. However, for fixed partial dentures, the technique used did not influence the misfit values, which were similar to

each other. Since CAD/CAM systems rely on complete digitized production technology, human interferences are eliminated and can increase the accuracy of adaptation of fabricated frameworks. In addition, the software used for planning with CAD/CAM systems presents a library of geometries supplied by the manufacturer of each implant. This library contains the design of each connection and can contribute to greater accuracy in the preparation of the prosthetic components that will be in direct contact with the implant platform. The use of a conventional method is predisposed to a greater number of interferences, correlated mainly with the manual skill and gualification of the professional executing it. However, for fixed implant-supported frameworks with more than one element, the situation becomes slightly different. The results found may be related to the fact that, while the accuracy of the casting technique for prostheses with more than one element will depend on the same variables presented for the single-unit restorations, the milling of these prostheses is subject to a greater number of interferences since they are milled in one-piece casting/monoblock. This significantly reduces the possibility of accurately reaching and reproducing the regions with the greatest richness of detail, such as the platform and design of the connection of an implant.

The subgroup analysis for the retention systems showed a statistical similarity in misfit values regardless of the manufacturing method used. The choice for the type of retention is based on the clinician's personal preference according to the clinical condition of the patient.^{48–50}

According to Michalakis et al⁴⁸ (2003), with respect to the retention systems, the prosthesis connection to the implants can be one of three different types: prosthesis screwed to the abutment (screw retained), prosthesis cemented to the abutment (cement retained), or prosthesis screwed or snap fit onto the implant directly (mechano-chemically [MC] retained). In the MC-retained system, the crown is chemically bonded (porcelain fired on the metal coping) over a metal substructure, which is later screwed or snap fit directly onto the implant.⁵¹

Screw retention systems are indicated when multiple abutments are provided to facilitate the insertion axis and removal of the prosthesis for cleaning or repair of possible damages such as loosening or fracture of the screws. The cemented systems are indicated in esthetic areas or situations in which problems with the angulation of the implants must be compensated.^{52–54} Moreover, when a screw-retained prosthesis is considered in an oral rehabilitation, it is recommended that a computerized surgical stent be used in addition to the splinted impression technique and the fabrication of a verification jig to achieve passive fit of the metal framework.⁵⁵

The literature has revealed that cemented prostheses may be more subject to the occurrence of biologic complications, whereas screw-retained prostheses present a greater tendency toward technical problems or failures.⁴⁸ However, knowing the greater reversibility of screw-retained prostheses, the technical or even biologic problems that may occur will be more easily solved compared to a cement-retained implant prosthesis.⁵⁶

It should be noted that internal misfit, no less important than marginal misfit, was also an initial objective of evaluation in this systematic review. However, only two among the eligible studies presented data regarding internal misfit and evaluation of the different methods.^{24,38} These results could not be grouped and compared, making a more detailed and reliable analysis of this question impossible. However, it should be noted that the internal adaptation of the prosthetic components could be directly related to the milling tip used by each milling system, and that the smaller the diameter of the tip, the better the reproduction of internal details of the implant-supported restorations, as well as the adaptation.^{38,57}

It is valid to observe at this moment that among the studies selected for this systematic review, there was great heterogeneity between the materials used for manufacturing frameworks with both techniques. The significance in the heterogeneity of the quantitative analysis represents a possible variability in the effects of the intervention in the selected studies. This could be related to a possible methodologic diversity between the studies, which compromises the high heterogeneity in the analysis.⁵⁸ However, because of this high heterogeneity, a random-effects model was used for the meta-analyses to minimize this influence. So, the results must be interpreted with caution and respecting the limitations of this study.

In addition, the limitations in terms of the different analysis methods for measuring the marginal misfit in the eligible studies can be an important factor that influenced the results. Due to the difficulty of conducting clinical studies to evaluate the marginal and internal misfit of implant-supported frameworks, this review was based only on in vitro studies. Thus, CAD/CAM is a viable clinical option for fabrication of implant-supported prostheses and components. However, further research is highly encouraged due to the low level of evidence observed in the selected studies.

CONCLUSIONS

Within the limitations of the eligible in vitro studies, the current systematic review shows that CAD/CAM systems resulted in improved marginal fit of frameworks over the conventional lost-wax casting technique for fabrication of single-unit frameworks. However, no difference was observed for the fixed implant-supported type or in terms of different retention systems.

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Appendix I

Excluded Studies and Reasons for Exclusion

Reason(s)	Reference
No control group	Karl et al ⁵⁹ Al-Abdullah et al ⁶⁰ Park et al ⁶¹ Katsoulis et al ⁶²
Volumetric analysis in mm ³	Almasri et al ⁶³ Drago et al ⁶⁴
Analyzed tooth-supported prostheses	Han et al ⁶⁵ Ueda et al ⁶⁶
Data of central point position at each implant analog	Paniz et al ⁶⁷
Incomplete data (no standard deviation)	Abdel-Azim et al ⁶⁸ Fernández et al ⁶⁹ Katsoulis et al ⁷⁰

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