

Clinical performance of monolithic CAD/CAM tooth-supported zirconia restorations: systematic review and meta-analysis

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Abstract

Purpose: The purpose of this systematic review was to evaluate the survival rate, biological complications, technical complications, and clinical behavior of single crowns supported by teeth made up in monolithic zirconia with CAD/CAM technology.

Study selection: An extensive electronic search was conducted through Medline/PubMed, Embase, and Cochrane Library databases. Additional manual search was performed on the references of included articles to identify relevant publications. Two reviewers independently performed the selection and electronic and manual search.

Results: From nine articles included, there was a total of 594 participants and 1657 single-tooth restorations with a mean exposure time of 1.07 years, and follow-up period between 0.3 and 2.1 years. All studies showed a moderate level of quality, with a consequent moderate possibility of associated bias, using the Newcastle-Ottawa Scale (NOS), with survival rate (SR) ranging between 91% to 100%. Bleeding on probing (BOP) were reported with an average value of 29.12%. Marginal integrity showed high success rate values for the observation periods, except for one that included patients with bruxism which obtained a SR of 31.60%. Failures and/or fractures, mostly total and requiring replacement, were observed in three studies. Linear regression showed that there was no statistical correlation between survival rate and type of cementation and the average years of follow-up ($p=0.730$ e $p=0.454$). There was high heterogeneity between studies ($I^2 = 93.74\%$ and $Q = 79.672$).

Conclusions: Within the limitation of this study, monolithic zirconia might be considered as a possible option for restoring single crowns, especially in the posterior zone.

Keywords: Computer-aided design, Zirconium oxide, Yttria-stabilized tetragonal zirconia, Tooth crown, Fixed partial denture.

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1. Introduction

In the last two decades, zirconia-based restorations have been increasingly used in Dentistry. Patients tend to choose metal-free restorations, preferring materials with similar properties to the natural teeth and similar characteristics of light scattering, achieving good esthetic results[1]. Polycrystalline ceramics, in which zirconia stands out, are ceramics that do not have glassy components, with a dense and cohesive structure that are very difficult to break and fracture[2]. Given those characteristics, Garvie et al. (1975)[3] entitled zirconia as “ceramic steel”. Then, considering that zirconia is the dental ceramic

material with the highest strength, it can be used as monolithic material, presenting notable advantages mainly related to the non-occurrence of chipping off a veneering ceramic and its numerous indications of use in single, partial, and full-mouth rehabilitation. Also, it presents high biocompatibility, less wear of the antagonist, easiness to polish, high hardness, low thermal conductivity, and chemical stability[4].

The emergence of these new materials like monolithic zirconia (MZ) combined with digital technology allows increasingly biomimetic results. In vitro studies showed superior performance and results regarding mechanical strength of MZ[5,6], allowing its use mainly for cases with unfavorable occlusion, parafunctional habits, previous fractures, and limited space for restorative materials[7].

However, clinical evidence of the existing literature on clinical performance and durability of this type of restorations is still scarce. There is a lack of clinical studies with a follow-up longer than five years,

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clinical randomized trials, and the absence of success rate studies of these crowns in the medium and long-term.

Thereby, it is essential that professionals can be able to access scientific evidence to make critical and rigorous decisions on oral rehabilitation treatment. Hence, the purpose of this systematic review and meta-analysis was to assess the survival rate, biological complications, technical complications, and clinical behavior of single teeth-supported monolithic zirconia crowns, developed with the CAD/CAM system, to help clinicians in the decision process.

2. Materials and Methods

This systematic review and meta-analysis was conducted following the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analysis)[8,9] and the research question was defined through the PICOT format (population, intervention, comparison, outcomes, and time)[10]. The protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews), CRD42020166112, organized by the Center for Reviews and Dissemination (University of York, National Institute for Health Research, United Kingdom).

The focused question was: "In an adult population, does monolithic zirconia restorations on natural teeth, in comparison when available with other type of material for crown rehabilitation, have superior survival rate and clinical results in a minimum 3 months follow-up?"

2.1. Information sources and search strategy

This electronic survey was initiated on 5 February 2020 and conducted until 10 May 2020 in three different databases, applying the English-language limitation: Medline/PubMed (National Library of Medicine), Embase, and Cochrane Library. At Medline/PubMed and Cochrane Library, different MeSH (medical subject headings) terms were combined by using Boolean operators AND, OR, and NOT (Supplementary Tables 1-3). A search was also carried out in the form of free text, using the search terms: "Monolithic zirconia"; "Monolithic dental crown"; "Zirconia dental crown" (Supplementary Table 3).

In the Embase database, a natural language search was performed also with Boolean operators AND and OR (Supplementary Table 4). Controlled language research was also carried out, combining the different Emtree terms (Embase subject headings), accompanied by the Booleans operators AND and OR, and using the same search terms. Combining research in controlled English-language at Embase, a total of 565 articles was obtained. For the selection of the studies, inclusion, and exclusion criteria were defined (Supplementary Table 5), such as only abstracts published in congress, e-posters, content non-published, gray literature, and letter to editor.

After eliminating duplicates, the titles and abstracts of all identified articles were systematically evaluated by two researchers (C.L. and L.A.). In situations where the relevance of a study was unclear, it was included for full-text reading and it was evaluated. Subsequently, the articles were read in full and the reasons for their exclusion were recorded. Any disagreement and/or discrepancy about the eligibility of the studies for this purpose was resolved with the presence of a third reviewer (A.C). Cohen's kappa value was calculated to measure inter-rater agreement in the study selection process.

2.2. Data extraction and method of analysis

Data extraction for descriptive and quantitative synthesis was performed using a standardized form and recorded in an Excel table (v.15.17 - Microsoft, Redmond, USA). The information extracted included: study (Authors/Year of publication), type of study, country, age, restorations (n), drop-outs (n), CAD/CAM system, monolithic zirconia type/brand, glaze/stain (yes or no), dental preparation, impression (digital/conventional), CAD/CAM system, cement/cementation process, follow-up period (years), evaluation system, location (anterior/posterior), dental group, whether in the maxilla or mandible, occlusal adjustments (yes or no), wear antagonist, absence or presence of plaque, surface treatment, marginal integrity, bleeding on probing (BOP), color stability (yes or no), dental vitality (n), number of failure (considered only fracture in which the material cannot be replaced or adjusted), and survival rate. In situations where the desired information about survival and/or failure rates was not present, it was excluded from the selection.

2.3. Statistical analysis method

This meta-analysis compared data obtained on success/survival rates after a minimum of three months in function. All analyzes were performed using Excel software (Microsoft, Redmond, USA), where the random effect model at a 5% significance level was used. To assess the quality of the cohort studies, the Newcastle-Ottawa Scale (NOS) for Quality Assessment was used. Heterogeneity among the studies was quantified using the Cochran test (Test Q) and the inconsistency test ($I^2 \geq 50\%$). Values above 75% (in both tests) were considered an indication of substantial heterogeneity, not allowing a fixed-effect analysis method to be applied (i.e., the effect of interest is not the same in all studies and therefore it is not possible to consider that the studies are homogeneous and derived from the same population)[11].

Since the confidence interval (CI) was not provided, the standard deviation (SD) value was used to calculate it. Linear regression (the relationship between survival rate, cementation, and average follow-up period) was also performed. Associated with this, a Q-Q graph (scatter diagram) was developed to compare two probability distributions. This means that, if the two sets of quantiles come from the same distribution, we must observe the points in the graph. If this line is approximately straight, we would be facing a normal distribution.

3. Results

3.1. Study Selection

Through the search strategy, 1298 references were initially identified (360 from Medline/PubMed, 373 from the Cochrane Library, and 565 from Embase). Of these, 224 duplicate articles were removed, resulting in a total of 1074 articles. Subsequently, through the selection by the inclusion and exclusion criteria (reading the title), 930 articles were eliminated, leaving a total of 144 articles. Of these, 13 articles were selected by abstract and four articles were eliminated after full read (Supplementary Table 6). The research flowchart and the identification process are schematically shown in **Figure 1** and Supplementary Table 6. Through a complete reading of the nine final articles, quantitative synthesis of them was carried out. Present information from the selected studies, such as study design, study objec-

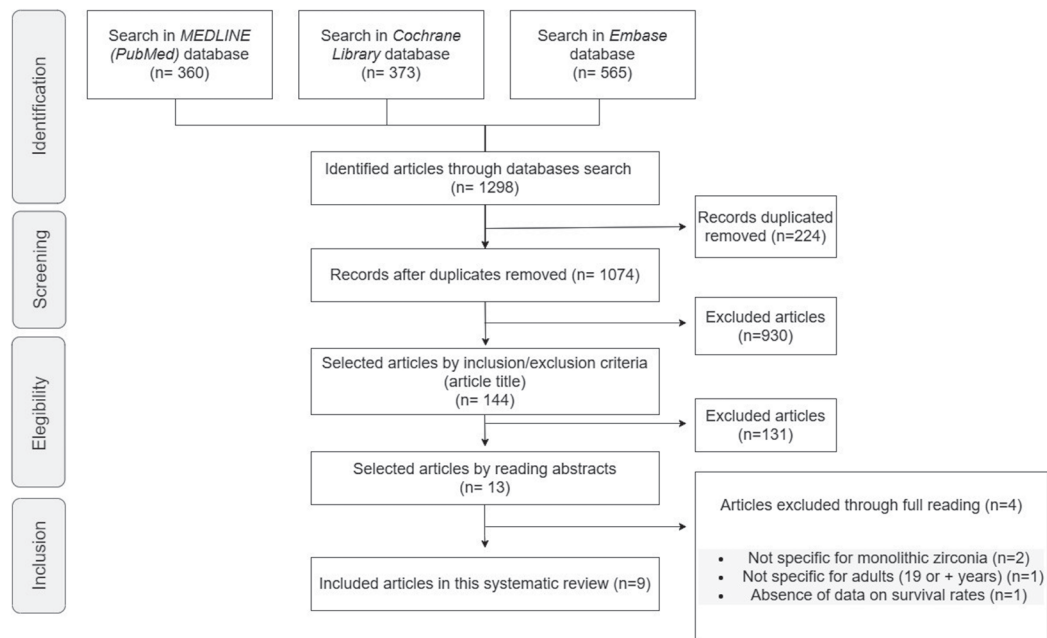


Fig. 1. Article selection strategy according to the PRISMA Flowchart (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

tive, sample size, evaluation methodology, and follow-up period are shown in **Table 1**.

3.2. Study characteristics

Descriptive analysis with total data, about follow-up time, type of study, tooth position, and patient characteristics are shown in Supplementary Table 7. In this quantitative analysis, 1657 monolithic zirconia unitary restorations were included. Most studies reported posterior mandibular restorations (premolars and molars), the majority of which (n=423) were maxillary restorations (n=380). The evaluated studies had an observation period between 0.3 and 2.1 years, with an average follow-up of 1.07 years. Thus, nine articles (1 randomized controlled trial[12]; 3 prospective cohort clinical trial[13–15]; 1 prospective observational case-series[16]; 2 retrospective clinical trial[17,18]; 1 retrospective observational clinical trial[19]; 1 retrospective observational case-series[20]) published between 2014 and 2019 were included in this systematic review (**Table 1**).

3.3. Inter-rater agreement

Cohen's kappa value was calculated to measure the inter-rater agreement in the study selection process. The standard deviation calculation was 0.98 (± 0.14) for the first selection stage and 0.78 (± 0.23) for the second stage, which represents an excellent and good agreement, respectively, between the two independent researchers (C.L. and L.A.). All disagreements were resolved by a third independent researcher (A.C.).

3.4. Patient characteristics

In this systematic review, a total of 594 individuals were reported, with an estimated average age of 49.1 years. These studies included 238 male patients and 316 female patients, with data about the patient's gender not being reported in three studies[12,13,20]. In ad-

dition, three studies[12,17,18] reported drop-outs of patients during the follow-up period, but only one article reported the associated causes[17]. The average number of patients who, for various reasons, could not be followed up was relatively low (9.7%, n=28). Of these, six patients were lost for the following reasons: one death, three housing changes, and two refusals to participate due to another disease[17].

3.5. Tooth preparation

Most of the dental preparations were made with the monolithic ceramic crowns' standard reductions (i.e., a minimum wall thickness of 1mm, occlusal reduction of 1.5 to 2.0mm, axial reduction of 1.0 to 1.5mm)[21].

3.6. Crown cementation

Konstantidinis et al.[13] refer to a pre-cementation treatment of the crown with an aluminum oxide blast (50 microns). Gunge et al.[18] refer to the application of a low pressure (0.6MPa) blasting of alumina and a 10-MDP primer (Clearfil® Ceramic Primer, Kuraray Noritake Dental Inc.) in the monolithic crown prior to its cementation.

In 6 of the 9 studies, the authors refer to the use of resin cement for the cementation of crowns[13–15,17–19]. One study reported the use of glass-ionomer cement and another one refers to the use of resin-modified glass ionomer cement[16]. The information about the cementation material was not available in 1 of the 9 studies included[20].

3.7. Clinical evaluation of the restorations

The quality assessment of the restorations was done with two different classifications. Thus, three articles[14–16] used the modified criteria of the California Dental Association (CDA) and four articles[12,13,18,20] used the modified criteria of the United States Public

Table 1. Data extraction table and descriptive analysis of the included articles.

Article (Authors/Year of publication)	Study type	Country	Age	Individuals (n)	Zirconia Restorations (n)	Drop-outs (n)	Type/Brand of Zircónia Monolítica
Konstantinidis et al. 2018	Pro	GR	49.52	65	65	s/d	Zenostar (Wieland, Canada)
Batson et al. 2014	Pro	US	s/d	22	10	13 (total)	Zenostar (Wieland, Canada)
Tang et al. 2019	Pro	CN	41.3	46	49	s/d	Zenostar (Wieland, Canada)
Kitaoka et al. 2018	Pro	JP	54	18	26	s/d	Aadva (GC Europe)
Gunge et al. 2018	Retro	JP	> 20 years	101	148	6	Cercon ht (Dentsply Sirona K.K.)
Zou et al. 2018	Retro	CN	37	289	321	s/d	YZ HT 40/19 (Vita Zahn-fabrik, Germany)
Hansen et al. 2018	Pro	NO	56.3	13	84	s/d	BruxZir (Glidewell Laboratories, USA)
Worni et al. 2017	Retro	SZ	59.1	40	238	6	Ceramill Zolid (Amann Girrbach)
Belli et al. 2015	Retro	GM	s/d	s/d	716	s/d	Zenostar (Ivoclar Vivadent, Liechtestein)

Pro= Prospective; Retro= Retrospective | s/d= No data | SA= No alterations | GR=Greece | GM= Germany | US= United States | CN = Canada | JP = Japan | NO=Norway | SZ= Switzerland.

Table 1 (cont.). Data extraction table and descriptive analysis of the included articles.

Article (Authors/Year of publication)	Dental preparation	Impressions (digital/ conventional)	CAD/CAM system	Cement/Cementing Process	Average Follow-up time (years)
Konstantinidis et al. 2018	Standard	Conventional	Zenotec CAM (Wieland Dental)	Resin cement	0.8
Batson et al. 2014	Standard	Digital	Mini-mill (Wieland Dental)	Glass Ionomer cement	0.3
Tang et al. 2019	Standard	Conventional	3Shape (Denmark)	Resin cement	0.8
Kitaoka et al. 2018	Standard	Conventional	Aadva Mill LD-1 (GC Europe)	Resin cement	0.9
Gunge et al. 2018	Minimum	Conventional	Cercon brain (Dentsply Sirona K.K.)	Resin cement	2.1
Zou et al. 2018	Endocrown	Digital	Cerec (Dentsply Sirona)	Resin cement	1.6
Hansen et al. 2018	s/d	s/d	s/d	Resin modified Glass ionomer cement	1.7
Worni et al. 2017	Standard	Conventional	Ceramill Motion 2 (Amann Girrbach)	Resin cement	2.0
Belli et al. 2015	s/d	Digital	Multiple Systems	s/d	0.3

s/d= No data.

Table 1 (cont.). Data extraction table and descriptive analysis of the included articles.

Article (Authors/Year of publication)	Evaluation system	Glaze/Stain (yes or no)	Location (anterior / posterior)	Dental Group	Site (maxilla)	Site (mandible)	Occlusal adjustments (yes or no)	Antagonist/Wear
Konstantinidis et al. 2018	USPHS	Yes	Posterior	PM/M	29	36	Yes	s/d
Batson et al. 2014	USPHS	Yes	Posterior	s/d	s/d	s/d	No (in 80%)	s/d
Tang et al. 2019	CDA	No	Posterior	M	24	25	Yes	No
Kitaoka et al. 2018	CDA	No	Posterior	PM/M	13	13	s/d	Yes (Crack in two antagonist teeth)
Gunge et al. 2018	s/d	Yes	Posterior	PM/M	71	77	Yes	No
Zou et al. 2018	USPHS	No	Posterior	M	157	165	Yes	s/d
Hansen et al. 2018	CDA	No	Anterior	Incisive/canine/PM	20	64	No	s/d
Worni et al. 2017	USPHS	Yes	Posterior/Anterior	Incisive/canine/PM/M	66	43	s/d	s/d
Belli et al. 2015	s/d	s/d	Posterior	PM/M	s/d	s/d	s/d	s/d

s/d= No data.

Table 1 (cont.). Data extraction table and descriptive analysis of the included articles.

Article (Authors/Year of publication)	Presence/Absence of Plaque	Surface treatment	Marginal integrity	Bleeding on Probing (BOP)	Color stability (yes or no)	Dental Vitality (n)	Failures (n)	Survival rate
Konstantinidis et al. 2018	Absence	s/d	93.80%	1.80%	No	19	0	100%
Batson et al. 2014	s/d	Final polishing	90%	SA	No	s/d	0	100%
Tang et al. 2019	Presence	Final polishing	100%	4.08%	Yes	s/d	1	93%
Kitaoka et al. 2018	Presence	Final polishing	88.46%	SA	No	3	0	100%
Gunge et al. 2018	s/d	Final polishing	s/d	s/d	s/d	0	1	91%
Zou et al. 2018	s/d	Final polishing	98.80%	s/d	Yes	0	0	100%
Hansen et al. 2018	Presence	Final polishing	31.60%	100%	Yes	s/d	1	98.81%
Worni et al. 2017	Presence	Final polishing	100%	10.60%	No	0	0	100%
Belli et al. 2015	s/d	Final polishing	s/d	s/d	s/d	s/d	0	100%

s/d= No data | SA= No alterations.

Health Service (USPHS). In two articles[17,19] the rating system was not mentioned.

Tang et al.[14], using the modified criteria of the California Dental Association (CDA), concluded that the survival parameters such as marginal adaptation, anatomic form, crown margin integrity, color match, and gross fracture did not show significant differences compared with the different time points ($P=.999$). Surface texture at different times did not change significantly ($P=.807$). Kitaoka et al.[15], according to the CDA quality evaluation, rated most crowns as “excellent” for marginal integrity and surface and “excellent” or “acceptable” for color and anatomical form. Only one crown was evaluated as a “correction” for color after placement.

Hansen et al.[16] evaluated the surfaces (using CDA criteria) and almost all crowns (90.5%) had excellent surfaces, the rest were evaluated as satisfactory. Besides that, the color was rated as satisfactory on all crowns. Most of the crowns (75.3%) had excellent shape whereas the remaining were evaluated as having a satisfactory shape. The crown margins were excellent on most of the crowns (66.8%) and satisfactory on the rest. Overall, all crowns were evaluated as 100% satisfactory and not in need of repair or remake regarding any of the CDA variables.

Using USPHS criteria, Konstantinidis et al.[13] concluded that at the 6- and 12-month examination all restorations (regarding the quality assessment) were rated either with Alpha or Bravo, except for one restoration which rated with Charlie for marginal discoloration. For the criteria “secondary caries” and “gross fracture” all crowns obtained an Alpha score.

This resulted in a success rate of 98.5%. The percentages of restorations with a B rating for marginal discoloration increased from 4.6% at the baseline to 16.88 at the 6- and 12-month examination. Regarding the “surface texture”, the B rating changed from 1.5% to 6.2% at the 6-month examination, and then remained at the same percentage at the 12-month examination. From the 6-month to the 12-month examination, most of the percentages of A and B rates did not change.

Batson et al.[12] within each USPHS criterion presented that Zr crowns were statistically significantly different from lithium disilicate (LD) and metal ceramic (MC) crowns for occlusion ($P<.001$). Eighty percent of Zr crowns had an “excellent” rating and needed no occlusal adjustment.

In the Zou et al.[19] study, the restorations were assessed using the United States Public Health Service (USPHS) criteria at 6 months, then 1, 2, and 3 years after treatment. The ratings for anatomic form, marginal adaptation, color match, marginal discoloration, surface roughness, and caries of the endocrowns proved to be practically unchanged compared with the high quality that was initially established. There were no significant differences in the repeated assessments for up to 3 years ($P>0.05$).

The records obtained by the USPHS by Worni et al.[17] revealed good clinical outcomes. While the scores for “color match” ($P<.001$) and “anatomical form” ($P=.005$) were different between the two examiners, no difference was found for marginal adaptation ($P=.71$). No secondary caries or loss of vitality of abutment teeth were recorded during the follow-up period.

3.8. Biological complications

The analysis of biological complications was performed using the following parameters: presence/absence of bacterial plaque, bleeding on probing, and dental vitality. When evaluating the studies, it can be seen that the presence of plaque was mentioned in four of them[14–17], with only one study reporting that the bacterial plaque was absent[13]. Bleeding on probing was reported in four studies[13,14,16,17] with an average value of 29.12%.

Regarding tooth vitality, it should be noted that a total of 22 prepared teeth were vital[13,15] and that in three studies[17–19], all teeth used had a root canal treatment. In a retrospective study by Gunge et al.[18], some biological complications were reported, although with a low prevalence (pulp complications: 2.03%; one fracture of the abutment tooth: 0.68%; and presence of secondary caries).

In the prospective study by Hansen et al.[16], visible plaque was found in two patients, and bleeding on probing was present in one or more teeth in all patients. According to Tang et al.[14], there was no incidence of secondary caries. However, at the end of the total follow-up period (96 weeks), 45 crowns had no plaque, three crowns had visible plaque and only one crown had a moderate plaque index at the level of the gingival margin.

3.9. Technical complications

The technical complications examined were: occlusal wear of the antagonist tooth, surface treatment, marginal integrity, failures/frac-

Table 2. Quality assessment of studies included at risk of bias using the Newcastle-Ottawa Scale.

Authors/Year	Konstantinidis et al. 2018	Batson et al. 2014	Tang et al. 2019	Kitaoka et al. 2018	Gunge et al. 2017	Zou et al. 2018	Hansen et al. 2018	Worni et al. 2017	Belli et al. 2015
Selection (up to 4*)	****	**	**	**	**	**	**	**	**
Comparability (up to 2*)					**		**		
Outcome/Exposure (up to 3*)	**	**	***	**	**	**	**	***	**
TOTAL	6/9	4/9	5/9	4/9	6/9	4/9	6/9	5/9	4/9
INTERPRETATION	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

1 to 3 – Low quality; 4 to 6 – Moderate quality; 7 to 9 – High quality of assessment.

tures, occlusal adjustments, and presence/absence of glaze/stain. Only Kitaoka et al.[15] reported two cracks in the antagonistic teeth. Regarding the surface treatment, most crowns were subjected to final polishing. Marginal integrity, in most studies, showed high success rate values for the observation periods. However, in the study by Hansen et al.[16], in which was included patients with bruxism, this value was relatively low (31.60%).

Failures/fractures, mostly total and requiring replacement, were observed in three out of nine studies[14,16,18]. In the retrospective study by Gunge et al.[18], with a survival rate of 91.5% after 3.5 years in clinical function, six monolithic zirconia crowns for natural teeth were lost, such as by hyperesthesia (1), root fracture of an abutment tooth (1), restoration fracture (1), pulpitis (2), and one restoration was removed because the tooth was used as an abutment tooth for a fixed partial denture after root fracture of an adjacent tooth, with other technical problems related to marginal discoloration, loss of retention and compromised esthetics being occasionally reported. Then, only 1 failure was really considered in this study[18] due to a direct failure/fracture of the restauration.

In the prospective study by Hansen et al.[16], only one complete fracture (1.19%) occurred after 16 months and was replaced by a new monolithic zirconia crown. This fracture was caused by a defect in the mesial margin of the crown. This author registered other technical findings/complications (e.g. marginal gap, overcountured, wear facet) but none caused the loss of the crown.

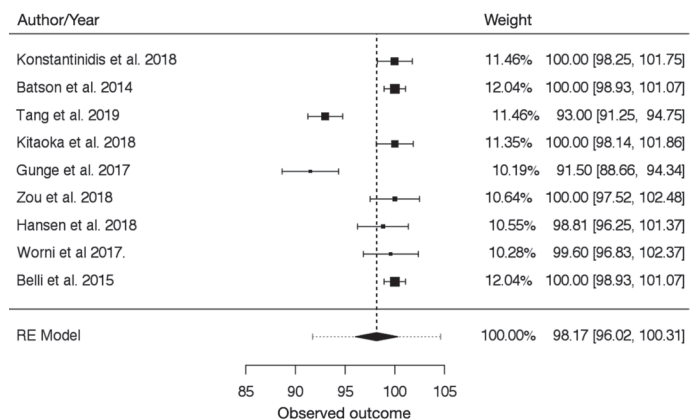
According to Tang et al.[14], the evaluated survival parameters (marginal adaptation, anatomical shape, marginal integrity, color stability, and surface texture) did not show significant changes between the different follow-up periods observed ($p=0.999$). Final occlusal adjustments were made to monolithic zirconia crowns in five studies, making a total of 593 crowns[12–14,18,19]. Glaze/stain was present in 461 restorations, being mentioned in four studies[12,13,17,18].

3.10. Survival rate (SR)

In order to assess the survival rate and clinical performance, and clinical behavior of monolithic zirconia single crowns supported by teeth made with CAD/CAM technology, this was defined as their permanence in situ (with or without modifications). The results obtained for the survival rate are shown in the results of the meta-analysis.

3.11. Quality of assessment and Statistical analysis

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of studies (Table 2). All studies showed a moderate level of quality, with the consequent moderate possibility of associated bias.

**Fig. 2.** Forest plot graph of survival rate in relation to the study analysis period.

Initially, an analysis of the SR was carried out, according to the observation period of the studies (Figure 2). Heterogeneity of 92.49% (I^2) and 81.518 (Q) was found. Through the analysis of the graphic, it was observed in two studies a lower survival rate[14,18], due to Gunge et al.[18] study, since it was the only work with the longest follow-up period and one of the largest crown samples ($n=148$). However, Tang et al.[14], with a relatively short period of analysis (0.8 years), presented a 93% survival rate.

Linear regression was performed, correlating SR with the type of cementation, and also with the average years of follow-up. The results showed that there was no statistical significance for these correlations (respectively, $p=0.730$ and $p=0.454$) (Supplementary Table 8). With these data, a Q-Q plot graph was developed, in which some points are represented alongside a line (with slight variations). However, they follow a distribution pattern considered normal (Supplementary Figure 1).

A forest plot graph was developed to analyze the SR concerning bleeding on probing, where there was high heterogeneity ($I^2=93.74\%$ and $Q=79.672$). The studies included were suggested to be within acceptable bleeding on probing (BOP) pattern which did not influence the survival rate of prosthetic rehabilitation. Only one study[13] showed an altered correlation due to high BOP (Figure 3).

The forest plot graphic analysis of the relationship between marginal integrity and SR (Figure 4) was done. It was found once again that only the article by Hansen et al.[16] presented marginal integrity as a risk factor that interfered with the SR of the restorations. This article was the same verified in the previous graph, which suggested this study is the main factor of heterogeneity.

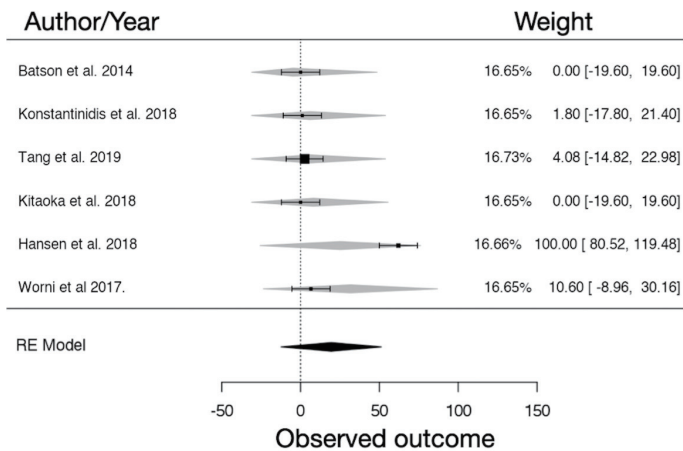


Fig. 3. Forest plot graph of the relationship between bleeding on probing and survival rate.

Linear regression was performed to verify statistically whether there was a significant difference between survival rate with BOP and marginal integrity. After data analysis, the correlation had a significant statistical difference, respectively, for BOP ($p=0.441$) and marginal integrity ($p=0.418$) (Supplementary Table 9).

Furthermore, it was performed the SR, according to the period of analysis, comparing the crowns produced with monolithic zirconia and other materials. However, only 2 out of 9 included studies[12,20] analyzed other materials, and one[20] out of 2 those articles, did not describe adequately the SR obtained for other materials, hampering the development of the statistical analysis. On the other hand, both confectioned the crowns digitally, for posterior teeth, and had a follow-up period of 3 months; one was a prospective[12] and another retrospective study[20]. From the baseline data found in the Batson et al.'s study[12], excluding the dropout due to this study did not inform the values after the occurrence of that, the monolithic zirconia crown had a SR of 90% (10% were unacceptable or rejected), 75% for metal-ceramic (MC), and 80% for lithium disilicate (LD).

4. Discussion

Systematic reviews and meta-analysis are usually assessed as high-quality scientific evidence, systematically identifying the relevant published information[10]. The introduction of new technologies, manufacturing processes, and materials in dental clinical practice should ideally be supported by scientific evidence. However, there is a lack of evidence on the clinical performance of monolithic ceramic (zirconia) crowns, which becomes necessary for more scientific studies with longer follow-up periods[22].

4.1. Biological complications

The main biological complications reported were increased BOP in the abutment teeth, secondary caries, bacterial plaque, loss of vitality, and fracture of the abutment tooth. However, it is worthy of note that the evidence is scarce in this regard since not all studies provided information and/or used different evaluation systems (USPHS or CDA).

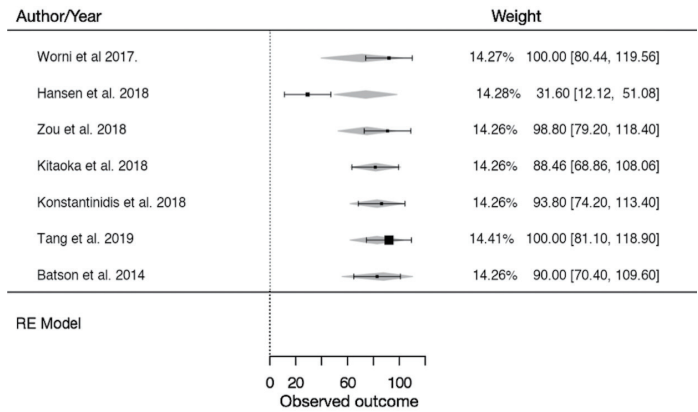


Fig. 4. Forest plot graph of the relationship between marginal integrity and survival rate.

After statistical analysis, it was also found that there was high heterogeneity, for survival rate ($I^2=92.49\%$ and $Q=81.518$) and the relationship between survival rate and BOP ($I^2=93.74\%$ and $Q=79.672$). Although BOP is mentioned in all articles, only one study was statistically significant (Hansen et al.[16]), showing interference between BOP and survival rate of monolithic zirconia crowns. In this study, it was verified that BOP was present in all patients, in more than one tooth.

MZ restoration usually has a polished surface, which facilitates cleaning by the patient avoiding the accumulation of biofilm, contributing to the maintenance of the health of the periodontal tissues[14]. In addition, it was reported in two articles[14,16] that patients were followed up by providing oral hygiene care during the observation period.

4.2. Technical aspects and complications

Regarding the reported technical complications, significant differences occurred in three studies[14,16,18], all with the occurrence of one fracture of MZ restoration - a total of three failures (0.18%). The lowest SR, according to statistical analysis, was found in two of these studies[14,18]. However, when analyzed Gunge et al.'s study[18], it was noticeable that, in addition to being the only work with an observation period greater than two years, it is also one of the studies with the largest number of samples ($n=148$). This may be a justification for the lowest survival found (91.5%).

Tang et al.[14] reported that, in one of the failures, the patient developed greater activity and masticatory strength on the rehabilitated side during the first four months, having reported contralateral tooth pain, a consequence of chronic pulpitis. Still, as an aggravating factor, this patient reported having preferably consumed harder foods. It was also mentioned that occlusal adjustments were made in all crowns, which can be a differentiating factor in the monitoring of rehabilitation and results in quality.

Currently and associated with CAD/CAM technology, it is possible to manufacture a wide variety of metal-free materials. Thus, the strength and stability of MZ have been tested in several in vitro investigations[23,24], which have shown restorations with overlay ceramics are more susceptible to wear when compared to polycrystalline ceramics[25–28].

Fractures associated with the material under analysis were observed in the study by Hansen et al.[16], which was predictable and expected by the authors, since the patients included in the study were grinding patients, presenting severe tooth wear (prior to restorative treatment), which may be a justification for the high heterogeneity found. Typically, these types of patients are excluded from studies that evaluate survival and/or failure rates. Thus, a higher failure rate would be previously expected in these patients, which is a limitation of the study.

Extreme tightening or defects in the crown margins may be possibly associated causes of fractures[29,30]. The manufacturing process may introduce defects in pre-cementation restoration, reducing the crown's resistance[29,30]. Also, the phenomenon of low-temperature degradation may be associated with this type of failure (since it spreads into the material)[29,30]. According to Nakamura et al.[31], this phenomenon, when associated with wear, can influence the quality of the surface, leading to an increase in the roughness. However, the clinical relevance of this phenomenon is still uncertain. Masticatory forces can also induce this phase transformation around surface microcracks; however, this is not likely to be the associated cause since, in most cases, time in function was relatively low[31].

4.3. Zirconia crown and tooth preparation

In the study by Zou et al.[19], in which they evaluated MZ molars endocrowns manufactured with CAD/CAM technology, the clinical success observed was 100% after three years in function. This contrasts with the results obtained in the systematic review[32], where endocrowns presented a high failure rate (2.56% per 100 restoration years). The concept of endocrown is related to microretention (through adhesion to dentin), gaining macro-retention and stability using available space within the pulp chamber[19]. The deeper the pulp cavity and its intracoronary extension, the greater the surface area that can be used for the retention and transmission of masticatory forces[33,34]. This could be the reason for the low survival rate of premolars endocrowns when compared to molars endocrowns, over a 12-year observation period[35].

Monolithic crowns have a high fracture resistance, allowing preparation without excessive tooth reduction, which is one of the reasons by which have become a treatment alternative to metal-ceramic or ceramic crowns[13]. Previous studies have shown that the design of the preparation influences significantly and is associated with fracture resistance of metal-ceramic crowns[6,34,36–38]. However, according to manufacturers' instructions, MZ crowns can be placed with a minimum thickness of 0.5mm[18]. Thus, many previous studies have evaluated zirconia strength with a thickness greater than 0.5mm, which allows its use in the molar teeth region, in terms of fracture resistance[34,36,38]. Previous studies have shown that monolithic zirconia crowns with a thickness greater than 1.0mm showed a high fracture resistance, being the same as that presented by metal-ceramic crowns[34].

Retention loss is significantly greater in zirconia-based restorations when compared to other types of restoration[39]. However, some studies report that crown retention depends on the mechanical roughness of the internal surface and chemical treatments with the adhesive monomer in zirconia primers[35,40]. An excellent reported option is related to the application of primers or adhesives containing monomers after blasting, allowing good adhesion to zirconia[41–43]. Only two studies mentioned a pre-treatment of the crown before ce-

mentation. In particular, Konstantidis et al.[13] referred to the use of an aluminum oxide blast (50 microns). Still, in Gunge et al.'s study[18], they applied a 10-MDP primer (Clearfil Ceramic Primer, Kuraray Noritake Dental Inc.) and low-pressure alumina blasting (0.6MPa) in the monolithic crown.

4.4. Occlusion and Marginal adaptation

Final occlusal adjustments were made to the MZ crowns in five studies, making a total of 593 monolithic crowns[12–14,18,19]. If minimal occlusal adjustments are necessary to optimize occlusal contact, the external surfaces of the MZ must be carefully polished to reduce any abrasive effects[44]. This is necessary because by making occlusal adjustments to the ceramic surface, microfractures can be created which can later develop into a total fracture[44]. Occlusal adjustments were required in two of the fractured restorations, which may have contributed to this event[14,18].

Regarding marginal adaptation, Hamza et al.[45] observed that different CAD/CAM systems have differences associated with marginal discrepancy and Kale et al.[46] showed that the marginal adaptation of monolithic crowns can be affected by the cementation process. In the analyzed articles, different CAD/CAM systems were used, with heterogeneity in the types of cement used, which can interfere with the marginal adaptation of the crowns. Despite the average preservation value of marginal integrity observed being high (86.09%), in the study by Hansen et al.[16], it decreased (31.6%). It is important to note that the protocol of this study did not consider the evaluation of the polymerization contraction of various types of cement under different polymerization conditions, as well as the compliance with the manufacturer's guidelines, regarding the selection and/or use mode, was not evaluated different types of cement. In the meta-analysis prepared in this study, a linear regression correlating the survival rate with the type of cementation, and with the average years of follow-up was performed. Through this, it was possible to conclude that there was no statistical significance between these correlations ($p=0.730$ and $p=0.454$, respectively).

In a systematic review elaborated by Boitelle et al.[47], they reported a lower adaptation value of the prosthetic structure when used CAD/CAM technology compared to conventional systems (gap less than 80µm between tooth and restoration surface). In addition, the full zirconia crown has high biocompatibility and CAD/CAM technology contributes to the design and manufacture of the crown providing excellent marginal adaptation[14].

4.5. Material surface

Regarding the antagonist wear, only in the Kitaoka et al.'s study[15], two cracks were observed in the antagonist teeth and, in the majority, the crowns were subjected to final polishing. According to Tang et al.[14], after the final polishing of monolithic zirconia ceramics, the average surface roughness reaches $0.17 \pm 0.07 \mu\text{m}$, this value being less than that presented by glazed zirconia ($0.69 \pm 4.10 \mu\text{m}$). Thus, the application of staining and glazing seems to increase the abrasiveness of this type of restoration[14].

The roughness of a surface is an essential factor for surface wear. A clinical study by Mundhe et al.[48] demonstrated that, during the one-year follow-up period, the attrition caused by the monolithic crown over the antagonistic natural tooth was $42.10 \pm 4.30 \mu\text{m}$ for premolars and $127.00 \pm 8.09 \mu\text{m}$ for molars ($p < 0.001$). In addition, it

has been shown by other studies that the attrition between monolithic crowns and natural teeth is similar to the wear between opposing enamel to metal-ceramic and enamel antagonists[49–51]. Still, another study has shown that, after two years of follow-up, the occlusal-cervical dimension of the antagonist tooth, MZ crown, and contralateral natural tooth decreased by 46µm, 14µm, and 19–26µm on average, respectively[52].

The results of the aforementioned studies showed that a polished monolithic zirconia crown causes less enamel attrition when compared to other ceramics[52]. Therefore, in light of these findings, a highly polished zirconia restoration is more desirable than glazed zirconia, causing less wear on the antagonist tooth[23,53–55].

4.6. Esthetic involvement

The esthetic aspect of MZ is still a challenge. According to Worni et al.[17] evaluating the MZ color is a process hampered by numerous conditions. Among them, we can mention the place luminous conditions, colors of adjacent reconstructions, and/or natural teeth. Since MZ is usually a monochromatic structure with an opaquer appearance, the lack of translucency and shiny opacity can prevent a natural and neutral integration between healthy and unrestored teeth, despite the individual glaze and stain[17]. By comparison, in a study by Haff et al.[56], 45% of acceptable color was reported in monolithic crowns, explained by the color difference between the restoration and adjacent tooth. Nowadays, the dental market presents polychromatic zirconia discs/blocs that may promote better esthetic results, but there is a need for clinical research on this issue.

4.7. Analysis of the quality and limitations of included studies

This systematic review had numerous limitations and/or associated implications. The main limitations are related to the methodology heterogeneity, different commercial brands of CAD/CAM and zirconia systems, and follow-up period. There was no established protocol concerning the esthetic and functional analysis of monolithic crowns and, therefore, this is one of the reasons for the high heterogeneity found in the included studies.

Newcastle-Ottawa Scale (NOS) showed that all studies included in this systematic review had a moderate quality of assessment, suggesting a moderate risk of bias. The limited number of patients involved (not representative of a general population) and crowns examined are limitations present in the studies included in this meta-analysis. Still, it is important to mention the workflow limitation, since not all studies refer to the impression conditions. In general, the impressions used were conventional, as mentioned in four[13–15,18] of the nine studies analyzed. Only one article did not mention the impression conditions[16]. Studies have shown that intraoral scanners appear to indicate greater and improved accuracy, whether in natural teeth or implants when compared to conventional impressions[57,58].

According to Miyazaki et al.[59], although the range of available ceramics has considerably improved its characteristics, zirconia is arguably the best all-ceramic material. Thus, due to the quick development of materials and processing technologies, the application of zirconia is promising. However, further studies and clinical evaluations are needed[59]. This is also an affirmation of a systematic review[60], implying zirconia as a clinical material of choice for molar zones (zone of increased occlusal forces). However, some concerns are still raised (requiring clinical evaluation), such as esthetic aspects

(related to color and respective antagonists), long-term chemical stability, or associated clinical wear[60].

4.8. Survival rate compared to different materials

In the retrospective study carried out by Belli et al.[20], evaluating the SRs of 35,000 posterior ceramic restorations, they concluded that after 3.5 years, the fracture rate was 1.4%. Also, it was shown that MZ restorations showed a clinical performance without any type of failure, in the first 8.5 months of placement. For different types of ceramics, a systematic review by Carvalho et al.[32] showed a lower failure rate, with statistical significance, for ceramics made with glass matrix when compared with polycrystalline ceramic restorations ($p < 0.001$; 1.18% versus 3.22%).

A meta-analysis study[60] revealed similar results, with a SR of 95.4% for fixed partial prostheses in zirconia-ceramic and 96.9% for metal-ceramic crowns, with no significant differences between the materials ($p=0.364$). However, according to the literature, the SR of fixed partial prostheses in zirconia-ceramic after 5 years is significantly lower, compared to metal-ceramics (92.1% and 94.7%, respectively) [39]. Although the SRs of most all-ceramic restorations are similar to those reported by metal-ceramic restorations, alumina, and leucite (or lithium disilicate) reported a 96% survival rate and 96.6%, respectively, being higher than zirconia and metal-ceramic. This is aligned with the findings of another systematic review[54] that demonstrated a high survival rate for single lithium disilicate crowns (97.8%) after 5 years in function. Feldspathic ceramics, despite their excellent esthetic properties, were those that had a lower survival rate (90.7%), limiting their application to the posterior sector[39].

In another study developed in 2014[61], concluded that MZ crowns exhibited greater fracture resistance when compared to lithium disilicate monolithic crowns, zirconia crowns with ceramic coating, and metal-ceramic crowns. Still, in this same study, it was concluded that MZ crowns with a thickness of 1.0mm, can present clinical results similar to metal-ceramic crowns. For this study, the observed average SR was 98.15%, with an average follow-up period of 1.07 years. It is a promising result, although with a short average follow-up period.

Considering the inherent limitations to this work, mostly related to the lack of well-standardized and reduced number of studies and controlled protocols, high heterogeneity, the reduced follow-up period, and the overall survival rate of zirconia monolithic restorations manufactured with CAD/CAM technology, this material might be a feasible option for restoration of single crowns, particularly in the posterior sector, however, must be observed the great number of limitations found. However, additional researches, preferably long-term randomized controlled studies, are required, using a larger sample of patients, to properly document the possible benefits of monolithic zirconia and assert its superiority when compared to other treatment alternatives.

Conflicts of Interest

All authors declare no conflict of interest associated to this article.

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Supplementary Table 1. Search equation used in Medline/PubMed and Cochrane Library.

Processing technology	Restoration material's properties	Type of Indirect Dental Restoration
"Computer-Aided Design"[Mesh]	AND "zirconium oxide" [Supplementary Concept] OR "yttria stabilized tetragonal zirconia" [Supplementary Concept] OR "In-Ceram Zirconia" [Supplementary Concept]	AND "Crowns"[Mesh] OR "Tooth Crown"[Mesh] OR "Denture, Partial, Fixed"[Mesh] NOT "Dental Implants"[Mesh] OR "Dental Implants, Single-Tooth"[Mesh]
(((("Computer-Aided Design"[Mesh]) AND ("zirconium oxide" [Supplementary Concept] OR "yttria stabilized tetragonal zirconia" [Supplementary Concept] OR "In-Ceram Zirconia" [Supplementary Concept])) AND ("Crowns"[Mesh] OR "Tooth Crown"[Mesh]) OR "Denture, Partial, Fixed"[Mesh]) NOT ("Dental Implants"[Mesh] OR "Dental Implants, Single-Tooth"[Mesh]))		

Supplementary Table 2. The research methodology used in Medline/PubMed.

Medline/PubMed*	
#1	"Computer-Aided Design"[Mesh]
#2	"zirconium oxide" [Supplementary Concept] OR "yttria stabilized tetragonal zirconia" [Supplementary Concept] OR "In-Ceram Zirconia" [Supplementary Concept]
#3	"Crowns"[Mesh] OR "Tooth Crown"[Mesh]
#4	"Denture, Partial, Fixed"[Mesh]
#5	"Dental Implants"[Mesh] OR "Dental Implants, Single-Tooth"[Mesh]
Search combination	#1 AND #2 AND (#3 OR #4) NOT #5
Applied filters	English, Humans, Adult: 19+years Types of studies: observational study; multicenter study; randomized controlled trial; evaluation studies: controlled clinical trials; comparative studies; clinical trial.
Total articles	259 articles (Results available on May 10 2020)

Supplementary Table 3. The research methodology used at Medline/PubMed.

Medline/PubMed*	
#1	Monolithic Zirconia
#2	Monolithic dental crown
#3	Zirconia dental crown
Search combination	#1 OR #2 OR #3
Applied filters	English, Humans, Adult: 19+years. Observational Study; Multicenter Study; Randomized Controlled Trial; Evaluation Studies; Controlled Clinical Trial; Comparative Study; Clinical Trial.
Total articles	101 articles (Results available on May 10, 2020)

Supplementary Table 4. The Research equation used at Embase.

Embase*	
#1	zirconium OR zirconia OR zirconium oxide
#2	'computer aided design/computer aided manufacturing' OR 'cad/cam software' OR cad cam OR 'computer aided design'
#3	crown OR 'tooth crown' OR 'fixed partial denture'
Research merging	#1 AND #2 AND #3
Total of articles	565 articles (Results available in 10 May 2020)
(zirconium OR zirconia OR zirconium oxide) AND ('computer aided design/computer aided manufacturing' OR 'cad/cam software' OR cad cam OR 'computer aided design') AND (crown OR 'tooth crown' OR 'fixed partial denture')	

Supplementary Table 5. Inclusion and Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
Published Articles in "Humans" (filter Species / Humans) "Humans" (filter Species/Humans)	Rehabilitated patients with partial crowns
Adult patients ("19+years")	Single monolithic ceramic crowns other than monolithic zirconia (e.g. feldspar ceramic or lithium disilicate)
Rehabilitated patients with monolithic zirconia CAD/CAM single crowns	Implant supported crown
Articles with data on survival and/or failure rates	Studies based on questionnaires, interviews, case reports and in vitro studies
Minimum three-month follow-up	

Supplementary Table 6. Studies excluded after full reading and the reason for their exclusion.

Authors, Year	Excluded studies and reason for exclusions
Esquivel Upshaw et al. 2018 ⁽⁷⁰⁾	Lack of data on survival rates
Donly et al. 2018 ⁽⁷¹⁾	Child population (between 3 and 7 years old)
Groten et al. 2010 ⁽⁷²⁾	Not specific for monolithic zirconia
Sagirkaya et al. 2012 ⁽⁷³⁾	Not specific for monolithic zirconia

Supplementary Table 7. Descriptive analysis: follow-up time, type of study, dental location, and patient characteristics.

Total	Restorations (n)	Average age (μ)	Individuals (n)	Follow-up (TT)	Follow-up (TM)	Study	Location	Failure (n)
	1657	49,1	594	10,5 years	1,07 years	Pro: 55,6% Retro: 44,4%	Anterior: 22,2%; Posterior: 88,9%	3

Supplementary Table 8. Linear regression of the correlation between survival rate and type of cementation and the average years of follow-up. Model Coefficients – Survival Rate

Predictors	Estimate	SE	t	p	Stand. Estimate
Cementation					
glass-ionomer - resin	-0.0315	0.0830	-0.379	0.730	-0.896
mean follow-up (y)	-0.1027	0.1198	-0.857	0.454	-1.926

Supplementary Table 9. Linear regression evaluating the survival rate with BOP (%) and marginal integrity.

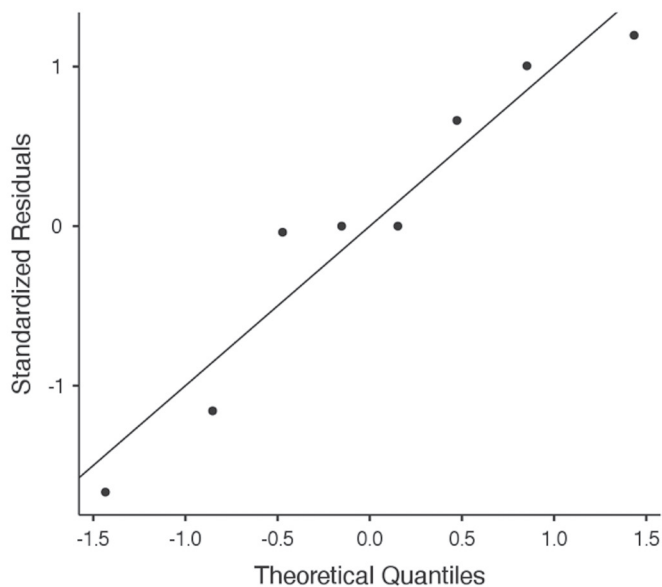
Model Fit Measures

Model	R	R ²	F	Overall Model Test		
				df1	df2	p
1	0.476	0.227	0.440	2	3	0.680

Model Coefficients - Survival rate (%)

Predictor	Estimate	SE	t	p
Intercept	116.343	19.074	6.100	0.009
Bleeding on probing (BOP)	-0.115	0.130	-0.887	0.441
Marginal integrity	-0.185	0.198	-0.937	0.418

Q-Q Plot

**Supplementary Figure 1** . Q-Q plot graph.