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REVIEW ARTICLE

WILEY CLINICAL ORAL IMPLANTS RESEARCH

Performance and outcome of zirconia dental implants in clinical studies: A meta-analysis

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Abstract

Objectives: To evaluate implant survival, peri-implant marginal bone loss, technical, and biological complications as well as aesthetic outcomes of zirconia implants in clinical studies.

Material and Methods: Electronic (Medline, Embase) and hand searches were performed to identify clinical studies published between January 2004 and March 2017 investigating zirconia dental implants with a mean follow-up of at least 12 months. Primary outcomes were implant survival and peri-implant marginal bone loss. Secondary outcomes included technical and biological complications as well as aesthetic outcomes. Meta-analyses were performed to estimate implant survival and marginal bone loss.

Results: From 943 titles, 264 abstracts were selected. Subsequently, 80 full-text articles were screened, and 18 studies were included for data extraction. One- (14 studies) and 2-piece zirconia implants (4 studies) were investigated. Commercially available (CA) (510 implants, 398 patients) and not commercially available (NCA) zirconia implants (618 implants, 343 patients) were identified. For CA implants (follow-up: 12–61.20 months), technical complications (1.6%), implant fractures (0.2%) and biological complications (4.2%) were reported. Meta-analyses estimated 1- and 2-year survival rates of 98.3% (95% CI: 97.0%–99.6%) and 97.2% (95% CI: 94.7%–99.7%), respectively, and a mean 1-year marginal bone loss of 0.7 mm (95% CI: 0.4–1.0 mm).

Conclusions: Since 2004, the survival rates of CA implants significantly improved compared with NCA implants. CA 1-piece zirconia implants showed similar 1- and 2-year mean survival rates and marginal bone loss after 1 year compared with published data for titanium implants. However, more clinical long-term data are needed to confirm the presently evaluated promising short-term outcomes.

KEYWORDS

biological complications, dental implants, aesthetics, implant survival, marginal bone loss, meta-analysis, prosthetics, soft tissue, technical complications, yttria stabilized tetragonal zirconia, zirconium oxide

1 | INTRODUCTION

Currently, titanium implants with a micro-rough surface are the "gold standard" in implant dentistry based on their excellent osseous integration, clinical reliability and scientific documentation (Buser et al., 2012; Cochran et al., 1996; Roehling, Meng, & Cochran, 2015). However, the initial period of implant dentistry dates back to when clinicians and scientists were already driven by the vision to achieve a more natural, tooth-like colored implant material. Thus, at the end of the 1960s, the first ceramic dental implants made from alumina were developed (Sandhaus, 1968), scientifically investigated and clinically used for a few decades until the early 1990s (De Wijs, Van Dongen, De Lange, & De Putter, 1994; Schlegel, Jacobs, & Leitenstorfer, 1994; Zetterqvist, Anneroth, & Nordenram, 1991). However, due to their poor biomechanical properties – alumina implants were prone to fracture when loaded extra-axially (Andreiotelli, Wenz, & Kohal, 2009) – these ceramic implants were finally removed from the market. At the beginning of the 1990s, a new material called "zirconium dioxide" (zirconia, ZrO_2) was introduced to dentistry. In comparison with other ceramics, zirconia shows superior biomechanical properties such as a high fracture toughness and bending strength (Christel, Meunier, Heller, Torre, & Peille, 1989) giving these implants the ability to withstand oral occlusal forces (Andreiotelli, Kohal, et al., 2009). Thus, zirconia is currently the material of choice for the fabrication of ceramic dental implants. As implant material, several advantages, such as its color, significantly reduced in vitro bacterial biofilm formation, and reduced numbers of inflammatory cells in the peri-implant soft tissues of healing caps and abutments have been reported for zirconia compared with titanium (Degidi et al., 2006; Roehling et al., 2017; Welander, Abrahamsson, & Berglundh, 2008). Equivalent to titanium, experimental studies have shown that increased surface roughness of zirconia implants is correlated with a higher degree of bone-to-implant contact and that micro-rough zirconia implants (Sa range 0.6–0.7 μm) show a comparable osseointegrative capacity to micro-rough titanium implants (Sa = 1.3 μm, Gahlert et al., 2007; Gahlert, Roehling, et al., 2012; Janner et al., 2018).

At the beginning of 2004, the first 1-piece zirconia dental implants were established on the market. Initially, creating micro-rough surface topographies without compromising the biomechanical stability of zirconia implants was a technical challenge. Thus, reduced survival rates and numerous zirconia implant fractures were reported for the first generation of zirconia implants (Gahlert, Burtscher, Grunert, Kniha, & Steinhauser, 2012; Gahlert et al., 2013; Osman, Swain, Atieh, Ma, & Duncan, 2014; Roehling, Woelfler, Hicklin, Kniha, & Gahlert, 2016). Since then, the industry has constantly improved manufacturing processes to gain micro-roughened zirconia implants with reliable fracture rates and fatigue strength. In addition, zirconia implants were developed not only in terms of the surface microstructure but also with regard to their macroscopic design. In contrast, the first zirconia implant systems were limited to a 1-piece design, and 2-piece zirconia implants with a cement- or screw-retained abutment and supra structures have also become available. Consequently, within the last 14 years, different zirconia implant generations with varying designs, diameters, physical properties and surface topography characteristics were introduced on the market. On the one hand, these developments have made zirconia implants a reliable treatment option with survival rates of more than 96% for an investigation period of 5 years (Grassi et al., 2015). On the other hand, the different implant generations can be confusing for the interpretation of published scientific data and for the clinical application of zirconia implants, which becomes even more relevant as most recently published systematic reviews and meta-analyses have pooled the available data on zirconia implants without considering the different physical properties and ongoing market availability of the investigated zirconia implants (Hashim, Cionca, Courvoisier, & Mombelli, 2016; Pieralli, Kohal, Jung, Vach, & Spies, 2017). Thus, the clinical relevance of the outcomes reported in the latter studies is rather controversial as only 5.3% (Hashim et al., 2016) and 55.3% (Pieralli et al., 2017) of the investigated implants were available on the market.

The objective of the present systematic review was to collect clinical data on zirconia implants with regard to survival rates, marginal bone loss, technical and biological complications as well as aesthetic outcomes. Moreover, the ongoing market availability of the investigated zirconia implants was considered for the first time to identify if significant changes regarding clinical outcomes have occurred over time.

2 | MATERIALS AND METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P (Moher et al., 2015)) statement using the Population, Intervention, Comparison and Outcome (PICO) method (Schardt, Adams, Owens, Keitz, & Fontelo, 2007). The protocol for this systematic review was registered on PROSPERO (CRD42016049624).

2.1 | Focused question

For the present review, the focused (PICO) question to be addressed was as follows: "In clinical studies, what are the outcomes of zirconia dental implants with regard to implant survival, peri-implant marginal bone loss, technical and biological complications as well as aesthetic outcomes?"

2.2 | Search strategy

An electronic, systematic search of the Medline via Pubmed and Embase via Elsevier databases was performed in March 2017. Articles in the English and German languages were included. For the literature search, clinical as well as preclinical studies were included. However, the present review includes only data from clinical studies. For the Medline search, the following terms and combinations were applied:

"Dental implants" [MeSH] OR "dental implantation" [MeSH] AND "zirconium oxide" [MeSH] OR "yttria-stabilized tetragonal zirconia" [MeSH] OR "zirconia" OR "zirconia implant*" OR "ceramic implant*" AND "osseointegration" [MeSH] or "bone-implant-interface" [MeSH] or "survival rate" [MeSH] or "success rate" or "marginal bone loss" or "soft tissue".

With regard to the Embase search, the following EMTREE words and combination were used:

"tooth implant" OR "tooth implantation" AND "zirconium oxide".

In addition to the electronic search, a hand search of the reference list of all included full-texts was performed.

For the electronic Medline search, reference management software (Endnote X 7.7.1, Thomson Reuters) was used. The obtained publications from the Embase search were also imported into the reference management software and finally screened.

2.3 | Inclusion criteria

For the systematic review, the following inclusion criteria were defined:

- Human trials investigating zirconia implants published between January 2000 and March 2017
- Studies at all levels of evidence, except expert opinion
- Case reports must include at least 10 patients
- Follow-up for at least 12 months
- Reported details regarding early and late implant failures
- Language: English, German

2.4 | Exclusion criteria

Studies not meeting the inclusion criteria were excluded from the review. Moreover, clinical studies investigating individually designed zirconia implants or multiple publications on the same patient population, as well as investigations based on charts, questionnaires or interviews, were excluded.

2.5 | Selection of studies

After elimination of duplicates, the reviewers (SR, MG) independently screened titles, abstracts and full-texts meeting the selection criteria. Unclear titles were included in the abstract screening. If titles or abstracts did not provide sufficient information for selection, full texts were obtained. Any disagreement with regard to inclusion and exclusion was resolved by discussion between the reviewers. To evaluate the agreement between the reviewers, Cohen's kappa coefficient (κ) was calculated for title and abstract selection (Landis & Koch, 1977).

2.6 | Data extraction and outcome measures

Data extraction by the reviewers was independently performed for all included studies (SR, MG) using data extraction tables. Disagreement with regard to data extraction was resolved by discussion. In case of missing or unclear information, the corresponding authors of the papers were contacted via email. If the information was still not sufficient for inclusion and evaluation, the study was excluded for the present review.

The timing of implant placement was classified as defined by Hammerle, Chen and Wilson (2004):

- Type 1: Immediate implant placement following tooth extraction.
- Type 2: Early implant placement after complete soft tissue healing (4–8 weeks)
- Type 3: Early implant placement after partial bone healing (12–16 weeks)
- Type 4: Late implant placement after complete bone healing (more than 16 weeks)

Implant loading protocols were classified as follows by Weber et al. (2009):

- Immediate loading: Functional loading of implants earlier than 1 week subsequent to implant placement
- Early loading: Functional loading of implants between 1 week and 2 months subsequent to implant placement
- Conventional loading: Functional loading after more than 2 months subsequent to implant placement

Implant failures were classified as follows:

- Early implant failures: Implant loss before prosthetic loading
- Late implant failures: Implant loss after prosthetic loading
- Implant fractures: Implant fracture after prosthetic loading

Technical complications were defined as abutment fracture, fracture of the implant prosthesis, chipping of the veneering ceramic and loosening of the implant prosthesis. Implant fractures were classified as an independent implant failure category and were not included in the technical complications.

The biological complications included bone loss of more than 2 mm over the observation periods, soft tissue complications (swelling, fistulas, mucositis) and peri-implantitis.

Aesthetic outcomes were evaluated using the pink aesthetic score (PES) according to Furhauser et al. (2005) or the papilla index according to Jemt (1997).

For all included clinical studies, the ongoing market clinical availability of the investigated zirconia implants was considered. Prototype zirconia implants that have never been commercially available or zirconia implant types or surface topographies that have been removed from the market while being further developed are defined in the text as "Not Commercially Available (NCA)" implants. Zirconia implant types and surface topographies that are still commercially available as investigated in the included studies are defined as "Commercially Available (CA)" implants.

From the included clinical full-text articles, the following data were extracted: author(s), year of publication, design of study (retrospective study design (RE)/prospective study design (PR)/randomized clinical trial (RCT)), number of included patients and implants, implant material (yttria-stabilized zirconia (YTZP)/alumina-toughened zirconia (ATZ),/titanium), implant design (1-piece/2-piece), implant system, implant surface treatment, surface roughness, market availability of investigated zirconia implant surface (yes/no), type of implant placement (Type 1/2/3/4), use of bone augmentation during surgery (yes/no), use of immediate temporization directly after implant placement (yes/no), immediate loading (yes/no), time period between implant placement and final prosthetic reconstruction (weeks), type of prosthetic restoration (single crown (SC)/fixed dental partials (FDP)/removable hybrid dentures (RHD)), retention modes prosthetics (abutments and prostheses, cement-retained (CR)/screw-retained (SR)), number of implant drop outs, number of early/late implant failures and implant fractures, mean observation period (months), implant survival (%) and mean peri-implant marginal bone loss (MBL, mm). Moreover, technical and biological complications as well as results regarding soft tissue aesthetics were recorded.

Primary outcomes were implant survival and peri-implant marginal bone loss (MBL). Secondary outcomes included technical and biological complications as well as aesthetic outcomes. In addition, the influence of the time point of implant placement, implant loading protocols, temporization, simultaneous bone augmentation during implant placement, implant bulk material (YTZP or ATZ), implant design, type of prosthetic reconstruction and market respectively clinical availability of the evaluated zirconia implants as confounding factors for implant survival and MBL were analyzed.

2.7 | Statistical analysis

For survival rates as well as for MBL after an observation period of 1 year, a random-effect meta-analysis was performed. The number of implants as well as standard errors, confidence intervals and weights depending on the final number of implants was included in the statistical analysis with regard to the estimation of survival rates. The amount of heterogeneity across studies was assessed with the I^2 measure (Higgins, Thompson, Deeks, & Altman, 2003). Unfortunately, not all studies reported confidence intervals, standard deviations or standard errors. To include these studies in the meta-analyses, standard errors where imputed by means of the reported standard errors and calculated standard errors from studies reporting either confidence intervals or standard deviations.

Forest plots were used for graphical presentations of the survival rates and MBL values in each study with confidence intervals and the weights given to each study in the meta-analyses, along with the overall pooled prevalence. In the graphs, the weight of each study included in the meta-analyses is represented by the area of a box with a center representing the size of the effect estimated from that study. The confidence intervals for the effect from each study are also shown. The summary effect is indicated by the middle of a diamond with left and right extremes representing the corresponding confidence interval.

In cases of evidence of heterogeneity in implant survival and MBL between studies, meta-regressions were used to analyze associations between survival and MBL and study characteristics. The estimated effects yielded evidence for the effects of time point of implant placement, implant loading protocols, temporization, simultaneous bone augmentation during implant placement, implant design, type of zirconia implant bulk material, type of prosthetic reconstruction and market clinical availability on survival and MBL. Both meta-analyses and meta-regressions were performed using STATA statistical software version 15.0 (StataCorp LLC, College Station, USA).

3 | RESULTS

The electronic database search resulted in 2,758 publications (Pubmed: 2304; Embase: 454, Figure 1). After removal of duplicates, 941 titles were available, and 2 additional studies were included after hand searching. Thus, the reviewers screened a total of 943 titles. The inter-examiner agreement for title selection was $\kappa = 0.9$, resulting in 264 abstracts for further evaluation. After screening the abstracts, a total of 80 publications were selected for full-text evaluation (inter-examiner agreement $\kappa = 0.8$). After analysis of the included full-text articles, a total of 18 clinical studies fulfilled the inclusion criteria and were included in the qualitative and quantitative analyses (Figure 1, Tables 1–4). Sixty-two reports had to be excluded (Table 5).

3.1 | Study characteristics

Of the 18 clinical studies that were included in the analysis (Tables 1–3), only 3 were prospective randomized clinical trials (RCT) that compared titanium ($n = 71$) and zirconia ($n = 89$, (Osman et al., 2014; Payer et al., 2015)) or immediately ($n = 20$) and conventionally ($n = 20$) loaded zirconia implants (Cannizzaro, Torchio, Felice, Leone, & Esposito, 2010). Fifteen publications reported observational studies. Of those, 11 were prospectively and 4 retrospectively designed (Table 1).

Most of the studies ($n = 14$) investigated 1-piece zirconia implants. Only 4 publications examined 2-piece zirconia implant systems (Table 1). When 2-piece implants were investigated, abutments as well as prosthetics were cement-retained (Table 2). With regard to zirconia implant diameter, the values ranged from 3.25 to 5.5 mm. Implant placement was performed immediately after tooth extraction (type 1), after soft tissue (type 2) or osseous healing (types 3 and 4, Table 2). In addition, immediate (2 studies) and conventional loading (16 studies) were applied (Table 2). Interestingly, 4 studies allowed early loading only for implants placed in the mandible, whereas conventional loading was applied for the maxilla (Jung et al., 2016; Spies, Balmer, Patzelt, Vach, & Kohal, 2015; Kohal, Knauf, Larsson, Sahlin, & Butz, 2012; Kohal, Patzelt, Butz, & Sahlin, 2013). The reported time periods between implant placement and installation of the final prosthetic reconstructions ranged between 6 and 30 weeks. Moreover, 14 studies allowed simultaneous bone regeneration during implant placement (Table 2). With regard to prosthetic reconstructions, the investigated implants were exclusively restored with SCs (10 studies, 452 implants), with SCs or FDPs (5 studies, 386 implants), exclusively with RHDs (1 study, 73 implants) or FDPs (1 study, 56 implants) and with SCs, FDPs, or RHDs (1 study, 161 implants, Table 2). Unfortunately, not every study provided detailed information regarding the implant diameter and distribution, type of implant placement and prosthetic reconstructions. Specific information in terms of the implant design was available for 17 studies investigating 890 1-piece and 117 2-piece zirconia implants (Table 1). In addition, 1 study investigated 121 1- and 2-piece zirconia implants. However, the authors did not provide detailed information regarding

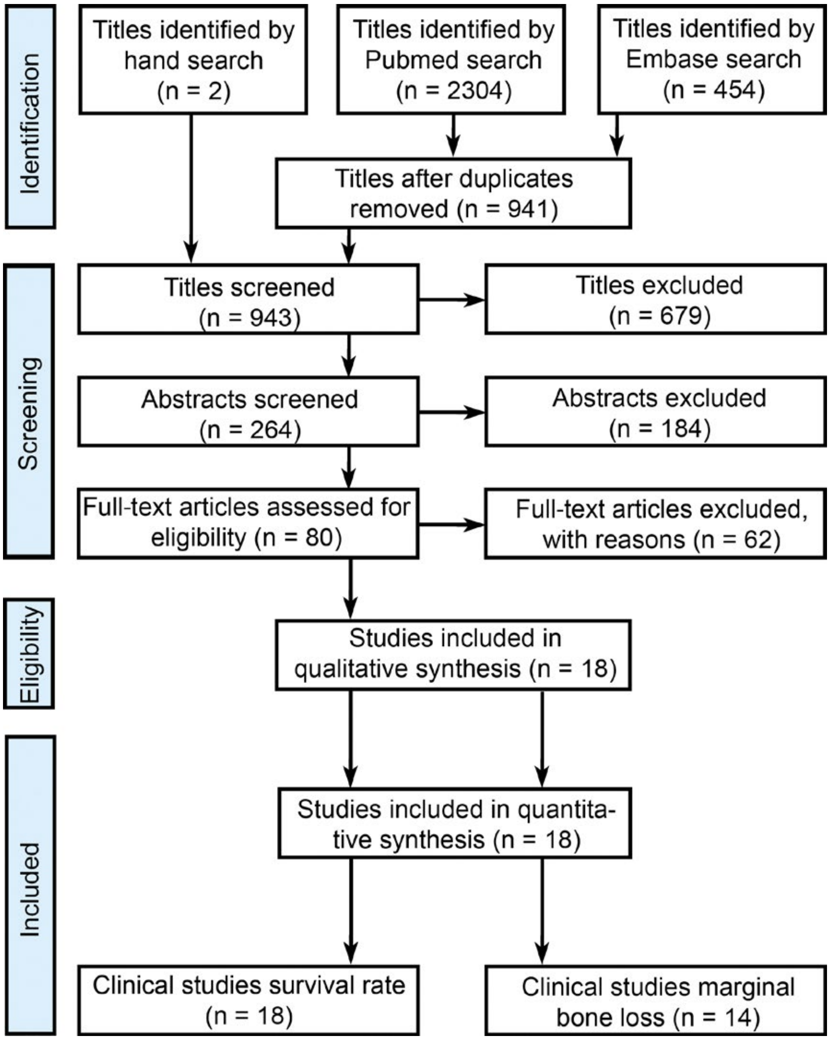

FIGURE 1 Search strategy and selection process for the included studies

the exact implant distribution (Brull, van Winkelhoff, & Cune, 2014). The evaluated zirconia implants were placed in a university setting (718 implants), in a private practice (334 implants) or in a multicenter setting consisting of university and private practice (76 implants, Table 1).

In 18 studies, 11 different zirconia implant types from 10 companies were evaluated. However, only 9 publications provided results for 5 types of CA zirconia implant surfaces: Zircon Vision: ZV 3, Straumann: PURE Ceramic Implant, Vita Zahnfabrik: Vitaclinical ceramic.implant, Bredent: Whitesky, Metoxit AG: Ziraldent (Table 1).

3.2 | Implant survival

Considering all included studies, data from 1,128 zirconia implants and 741 patients were included in the present review with regard to implant survival. A total of 21 patients (2.8%) and 55 zirconia implants (4.9%) were reported as dropouts (Table 3). Overall, 44 implants were reported as early failures (3.9%), 19 implants as late failures (1.7%) and 22 implants as fractures (2.0%). Thus, 7.5% of all investigated implants failed. Six studies provided detailed information regarding reasons for early and late implant failures. Interestingly, in the latter studies, implant mobility without any clinical signs of infection was reported as a reason for early and late failures (Brull et al., 2014; Cannizzaro et al., 2010; Cionca, Muller, & Mombelli, 2015; Kohal et al., 2012, 2013; Roehling et al., 2016).

3.2.1 | NCA zirconia implants

Nine studies reporting data on 618 implants and 343 patients were included (Table 1). The survival rates ranged between 71.2% and 100% for an overall mean observation period of 6 years (range 12–71 months, Table 3). Overall, 11.8% (73 implants) zirconia implants failed (5.8% early failures (36 implants), 2.6% late failures (16 implants), 3.4% fractures (21 implants)).

Two randomized clinical trials directly compared the clinical performance of titanium and zirconia implants. In detail, Payer et al. (2015) investigated 2-piece zirconia and 2-piece titanium implants with cement-retained SCs. Thirty months after implant placement, survival rates of 93.3% and 100% were reported, respectively. In addition to that, Osman et al. (2014) stabilized RHDs on 73 1-piece zirconia and 56 titanium implants in 24 edentulous patients.

TABLE 1 Clinical studies investigating implant survival. Impl: Implants; Impl. Design: Implant Design, 1: 1-piece implant design; 2: 2-piece implant design; Univ.: University; Priv. pract.: Private practice; Ti: Titanium; YTZP: yttria-stabilized zirconia; ATZ: alumina-toughened zirconia; PR: prospective study design; RE: retrospective study design; RCT: randomized clinical trial; NR: not reported

Author/year	Study design	Patients (n)	Impl. (n)	Material	Impl. design	Setting	Company/Implant type	Surface treatment	Surface roughness (μm)
Hollander et al. (2016)	RE	38	106	YTZP	1	Univ.	Z-Systems/Z-Look3	Sandblasting	0.5 < Ra < 3–5
Roehling et al. (2016)	RE	71	161	YTZP	1	Priv. pract.	Z-Systems/Z-Look3	Sandblasting	0.5 < Ra < 3–5
Cionca et al. (2015)	PR	32	49	ATZ	2	Univ.	Dentalpoint/Zeramex T (ZERAFIL 3)	Sandblasting, acid etching	NR
Mellinghoff et al. (2015)	RE	23	51	YTZP	1	Priv. pract.	Z-Systems/Z-Look3 Evo	Sandblasting	0.5 < Ra < 3–5
Payer et al. (2015)	RCT	22	16	YTZP	2	Univ.	Ziterion/Vario z	Sandblasting	NR
			15	Ti	2		Ziterion, Vario t	Sandblasting, Bonit® coating	NR
Osman et al. (2014)	RCT	12	73	YTZP	1	Univ.	Southern Implants	Acid etching	Ra 1–2
		12	56	Ti	1		Southern Implants	Sandblasting, acid etching	Ra 1–2
Kohal et al. (2013)	PR	28	56	YTZP	1	Univ.	Nobel Biocare/ZiUnite	Sintering with rough pore former	Sa 1.24
Kohal et al. (2012)	PR	65	66	YTZP	1	Univ.	Nobel Biocare/ZiUnite	Sintering with rough pore former	Sa 1.24
Cannizzaro et al. (2010)	RCT	20	20	YTZP	1	Priv. pract.	Z-Systems/Z-Look3	Sandblasting	0.5 < Ra < 3–5
		20	20	YTZP	1		Z-Systems/Z-Look3	Sandblasting	0.5 < Ra < 3–5
Becker et al. (2017)	PR	52	52	YTZP	2	Univ.	Zircon Vision/ZV3	Air particle abrading, sintering	Ra 7.0
Kniha et al. (2017)	PR	62	66	YTZP	1	Priv. pract.	Straumann/PURE Ceramic Implant	Sandblasting, acid etching	Sa 0.70
		16	16	YTZP	1		Straumann/PURE Ceramic Implant	Sandblasting, acid etching	Sa 0.70
Gahlert et al. (2016)	PR	44	44	YTZP	1	Priv. pract. and Univ.	Straumann/PURE Ceramic Implant	Sandblasting, acid etching	Sa 0.70
Jung et al. (2016)	PR	60	71	YTZP	1		Vita Zahnfabrik/ceramic. implant	Sandblasting, acid etching	Ra 1.2
Grassi et al. (2015);	PR	17	16	YTZP	1	Priv. pract.	Bredent/WhiteSky	Sandblasting	Sa 1.17
		17	16	YTZP	1	and Univ.	Bredent/WhiteSky	Sandblasting	Sa 1.17
Spies, Balmer, et al. (2015)	PR	40	53	ATZ	1	Univ.	Metoxit AG/Ziraldent FR 1	Sintering with pore-building polymers	Ra 1.8
Brull et al. (2014)	RE	74	121	YTZP	1, 2	Univ.	Zircon Vision/ZV 3	Air particle abrading, sintering	Ra 7.0
Borgonovo, Censi, et al. (2013)	PR	13	35	YTZP	1	Univ.	Bredent/WhiteSky	Sandblasting	Ra 0.9–1.0
Payer et al. (2013)	PR	20	20	YTZP	1	Univ.	Bredent/WhiteSky	Sandblasting	Sa 1.17

Yellow background: NCA zirconia implants.
White background: CA zirconia implants.

TABLE 2 Clinical studies investigating implant survival. Ti: Titanium; YTZP: yttria-stabilized zirconia; ATZ: alumina-toughened zirconia; SC: single crowns; FDP: fixed dental partials; RHD: removable hybrid denture; CR: cement-retained; SR: screw-retained; RM: removable

Author/year	Material	Type implant placement	Simultaneous bone augmentation	Immediate temporization	Immediate loading	Time period placement – final reconstruction (weeks)	Prosthetics	Retention modes prosthetics (abutments/prostheses)
Hollander et al. (2016)	YTZP	NR	NR	No	No	Maxilla: 24 Mandible: 16	SC, FDP	–/CR; –/CR
Roehling et al. (2016)	YTZP	2,3,4	Yes	No	No	12	SC, FDP, RHD	–/CR; –/CR; –/RM
Cionca et al. (2015)	ATZ	3,4	Yes	No	No	12	SC	CR/CR
Mellinghoff et al. (2015)	YTZP	NR	No	No	No	Maxilla: 24 Mandible: 12	SC	–/CR
Payer et al. (2015)	YTZP	4	No	No	No	Maxilla: 24 Mandible: 16	SC	CR/CR
	Ti	4	No	No	No	Maxilla: 24 Mandible: 16	SC	SR/CR
Osman et al. (2014)	YTZP	4	Yes	Yes	No	16	RHD	–/RM
	Ti	4	Yes	Yes	No	16	RHD	–/RM
Kohal et al. (2013)	YTZP	1,2,3,4	Yes	Yes	No	Maxilla: 14 Mandible: 6	FDP	–/CR
Kohal et al. (2012)	YTZP	1,2,3,4	Yes	Yes	No	Maxilla: 14 Mandible: 6	SC	–/CR
Cannizzaro et al. (2010)	YTZP	1,2,3,4	Yes	Yes	Yes	18	SC	–/CR
	YTZP	1,2,3,4	Yes	Yes	No	18	SC	–/CR
Becker et al. (2017)	YTZP	2,3,4	Yes	No	No	Maxilla: 12 Mandible: 10	SC	CR/CR
Kniha et al. (2017)	YTZP	3,4	Yes	No	No	12	SC	–/CR
	YTZP	1	Yes	Yes	No	12	SC	–/CR
Gahlert et al. (2016)	YTZP	2,3,4	Yes	No	No	26	SC	–/CR
Jung et al. (2016)	YTZP	NR	Yes	Yes	No	Maxilla:16 Mandible: 8	SC, FDP	–/CR; –/CR
Grassi et al. (2015)	YTZP	1	Yes	Yes	Yes	14	SC	–/CR
	YTZP	4	Yes	Yes	Yes	14	SC	–/CR
Spies, Balmer, et al. (2015)	ATZ	1,2,3,4	Yes	Yes	No	Maxilla: 14 Mandible: 6	SC, FDP	–/CR; –/CR
Brull et al. (2014)	YTZP	1,2,3,4	Yes	No	No	18.4	SC, FDP	CR/CR; CR/CR
Borgonovo, Censi, et al. (2013)	YTZP	NR	Yes	Yes	No	24	SC, FDP	–/CR; –/CR
Payer et al. (2013)	YTZP	3,4	No	Yes	No	16	SC	–/CR

Yellow background: NCA zirconia implants.
White background: CA zirconia implants.

TABLE 3 Clinical studies investigating implant survival. Impl: Implants; Ti: Titanium; YTZP: yttria-stabilized zirconia; ATZ: alumina-toughened zirconia; NR: not reported

Author/year	Impl. (*n*)	Material	Follow-up after placement (months)	Drop Outs Implants (*n*)	Early failures (*n*)	Late failures (*n*)	Fractures (*n*)	Survival rate (%)	Mean MBL (mm)
Hollander et al. (2016)	106	YTZP	14.25	–	0	0	0	100	NR
Roehling et al. (2016)	161	YTZP	71.28	–	14	4	18	77.3	0.97 ± 0.07
Cionca et al. (2015)	49	ATZ	19.32	2	1	5	0	87.3	≤1
Mellinghoff et al. (2015)	51	YTZP	29.08	0	0	0	0	100	0.63 ± 0.94
Payer et al. (2015)	16	YTZP	30	0	0	1	0	93.3	1.38 ± 0.86
	15	Ti	30	0	0	0	0	100	1.27 ± 0.43
Osman et al. (2014)	73	YTZP	16	7	12	6	3	71.2	0.42 ± 0.4
	56	Ti	16	27	2	8	0	82.1	0.18 ± 0.47
Kohal et al. (2013)	56	YTZP	12	0	1	0	0	98.2	1.95 ± 1.71
Kohal et al. (2012)	66	YTZP	12	1	3	0	0	95.4	1.31 ± 1.49
Cannizzaro et al. (2010);	20	YTZP	12	0	3	0	0	85	0.9 ± 0.48
	20	YTZP	12	0	2	0	0	90	0.72 ± 0.59
Becker et al. (2017)	52	YTZP	24	4	0	2	0	95.8	NR
Kniha et al. (2017)	66	YTZP	15	0	0	0	0	100	NR
	16	YTZP	15	0	0	0	0	100	NR
Gahlert et al. (2016)	44	YTZP	12	2	1	0	0	97.6	1.02 ± 0.9
Jung et al. (2016)	71	YTZP	16	3	1	0	0	98.6	0.78 ± 0.79
Grassi et al. (2015)	16	YTZP	61.2	1	1	0	0	93.3	1.29 ± 0.25
	16	YTZP	61.2	0	0	0	0	100	1.17 ± 0.33
Spies, Balmer, et al. (2015)	53	ATZ	36	1	3	0	0	94.2	0.79 ± 0.67
Brull et al. (2014)	121	YTZP	18.4	–	1	1	1	96.5	0.13 ± 0.6
Borgonovo, Censi, et al., 2013	35	YTZP	48	7	0	0	0	100	1.63
Payer et al. (2013)	20	YTZP	24	0	1	0	0	95	1.29 ± 1

Yellow background: NCA zirconia implants.
White background: CA zirconia implants.

TABLE 4 Technical and biological complications. Impl: Implants; NA: not applicable due to 1-piece implant design; NR: not reported

Author/year	Impl. (*n*)	Chipping (*n*)	Decementation (*n*)	Abutment fracture (*n*)	Bone loss >2 mm (*n*)	Soft tissue complications (*n*)	Peri-implantitis (*n*)
Hollander et al. (2016)	106	NR	NR	NA	NR	0	0
Roehling et al. (2016)	161	NR	NR	NA	0	0	0
Cionca et al. (2015)	49	0	0	2	0	0	0
Mellinghoff et al. (2015)	51	3	0	NA	0	NR	0
Payer et al. (2015)	31	NR	NR	NR	0	NR	0
Osman et al. (2014)	129	NR	NR	NA	0	NR	0
Kohal et al. (2013)	56	NR	NR	NA	22	0	0
Kohal et al. (2012)	66	NR	NR	NA	27	0	0
Cannizzaro et al. (2010)	40	1	1	NA	0	1	0
Becker et al. (2017)	52	0	0	1	NR	NR	18
Gahlert et al. (2016)	44	NR	NR	NA	0	NR	0
Jung et al. (2016)	71	0	0	NA	0	0	0
Grassi et al. (2015)	32	NR	NR	NA	0	0	0
Spies, Balmer, et al. (2015)	53	NR	NR	NA	0	0	0
Brull et al. (2014)	121	NR	NR	NR	0	0	0
Borgonovo, Censi, et al. (2013)	35	NR	NR	NA	0	0	0
Payer et al. (2013)	20	NR	NR	NA	0	NR	0

Yellow background: NCA zirconia implants.
White background: CA zirconia implants.

However, the authors used a novel, unestablished surgical protocol combining alveolar and palatal implants in the maxilla. Thus, 16 months after implant placement, survival rates 82.1% for titanium and of 71.2% for zirconia were observed. Additionally, when comparing different loading protocols for 1-piece zirconia implants restored with cement-retained SCs, decreased survival rates were reported for immediately (85%) compared to conventionally loaded (90%) implants at 12 months after placement (Cannizzaro et al., 2010).

Considering NCA zirconia implants, the meta-analysis estimated a 1-year zirconia implant survival rate of 91.2% (CI 85.7–96.6). For the included studies, a high degree of heterogeneity was evaluated (I^2 = 96.4%, p < 0.01, Figure 2).

3.2.2 | CA zirconia implants

A total of 510 zirconia implants and 398 patients were investigated in 9 studies (Table 1). The reported survival rates ranged from 93.3% to 100% for mean follow-up periods between 12 and 61.20 months (5.10 years, Table 3). Overall, 12 implants (2.4%) failed (early failures: 8 implants (1.6%), late failures: 3 implants (0.6%), fractures: 1 implant (0.2%)).

Two prospective observational studies evaluated different surgical protocols. In detail, Grassi et al., 2015 investigated the clinical performance of immediately loaded 1-piece zirconia implants restored with cement-retained SCs either placed in postextraction (type 1) or in healed sites (type 4). The authors reported 1 early failure only in the

TABLE 5 Excluded studies

Reason for exclusion	Number	Studies
Studies investigating alumina dental implants	2	Pigot, Dubruille, Dubruille, Mercier, and Cohen (1997), Stuge and Ellingsen (1991)
Review articles	19	Andreiotelli, Wenz, et al. (2009), Apratim et al. (2015), Buser, Sennerby, and De Bruyn (2017), Chen, Moussi, Drury, and Wataha (2016), Depprich et al. (2014), Elnayef et al. (2017), Hashim et al. (2016), Hisbergues, Vendeville, and Vendeville (2009), Hobkirk and Wiskott (2009), Kohal, Att, Bächle, Butz, and Author (2008), Kumar, Jain, Jayesh, Parthasaradhi, and Venkatakrishnan (2015), Ozkurt and Kazazoglu (2011), Özkurt and Kazazoĝlu (2010), Pieralli et al. (2017), Prithviraj, Deeksha, Regish, and Anoop (2012), Regish, Sharma, and Prithviraj (2013), Van Dooren et al. (2012), Vohra et al. (2015), Wenz, Bartsch, Wolfart, and Kern (2008)
Case reports/case series of less than 10 patients	12	Arnetzl et al. (2010), Aydin, Yilmaz, and Ata (2010), Aydin, Yilmaz, and Bankoglu (2013), Bankoglu Gungor, Aydin, Yilmaz, and Gul (2014), Borgonovo, Boninsegna, Dolci, Ghirlanda, and Censi (2010b), Kohal and Klaus (2004), Mehra and Vahidi (2014), Oliva, Oliva, and Oliva (2008a,b, 2010b), Parmigiani-Izquierdo, Cabana-Munoz, Merino, and Sanchez-Perez (2017), Sierraalta and Razzoog (2009)
Clinical studies investigating root shaped, individually designed zirconia implants	6	Nair, Prithviraj, Regish, and Prithvi (2013), Patankar, Kshirsagar, Patankar, and Pawar (2016), Pirker and Kocher (2008, 2009, 2011), Pirker, Wiedemann, Lidauer, and Kocher (2011)
Clinical studies: Multiple publications on the same patient population	14	Borgonovo et al. (2011), Borgonovo, Arnaboldi, Censi, Dolci, and Santoro (2010), Borgonovo et al. (2015), Borgonovo, Corrocher, et al. (2013) Borgonovo, Fabbri, Vavassori, Censi, and Maiorana (2012), Borgonovo, Vavassori, et al. (2013), Gahlert, Burtscher, et al. (2012); Gahlert et al. (2013), Kniha et al. (2016), Oliva, Oliva, and Oliva (2007), Osman and Ma (2014), Osman, Payne, Duncan, and Ma (2013), Siddiqi, Kieser, De Silva, Thomson, and Duncan (2015), Spies, Sperlich, Fleiner, Stampf, and Kohal (2016b)
Clinical studies only investigating prosthetic outcomes and not zirconia implant survival	4	Spies, Kohal, Balmer, Vach, and Jung (2017), Spies, Patzelt, Vach, and Kohal (2016), Spies, Stampf, and Kohal (2015), Spies, Witkowski, Butz, Vach, and Kohal (2016)
Data not clear for evaluation	4	Blaschke and Volz (2006), Lambrich and Iglhaut (2008), Mellinghoff (2006), Oliva, Oliva, and Oliva (2010a)
Publications based on charts, questionnaires or interviews	1	Jank and Hochgatterer (2016)

postextraction group. Thus, after a mean follow-up period of more than 5 years after placement (mean 61.2 months), survival rates of 93.3% and 100% were evaluated for type 1 and type 4 implant placement, respectively (Grassi et al., 2015). In contrast, equivalent survival rates (100%) were reported 15 months after implant placement for 1-piece zirconia implants restored with cement-retained SCs when type 1 or type 3 and 4 implant placements were applied (Kniha et al., 2017).

When considering CA zirconia implants, the meta-analysis estimated a 1-year survival rate of 98.3% (CI 97.0–99.6). For the evaluated studies, a moderate degree of heterogeneity was estimated (I^2 = 52.7%, p = 0.02, Figure 2). CA zirconia implants showed statistically significantly increased implant survival rates compared with NCA zirconia implants (p = 0.028).

The meta-regression for CA zirconia implants showed that type 1 implant placement, immediate temporization, immediate loading and simultaneous bone augmentation procedures did not have any significant effect on the reported 1-year survival rates (p > 0.05, Figure 3). Moreover, studies that evaluated SCs and FDPs showed similar survival rates compared to studies exclusively investigating SCs (p > 0.05, Figure 4). Interestingly, the meta-regression estimated higher survival rates for YTZP compared with ATZ and for 1-piece compared with 2-piece zirconia implants. However, these differences were not statistically significant (p > 0.05, Figure 3).

For a reduced number of studies reporting data for 192 implants and 159 patients, a 2-year meta-analysis could be performed (Becker et al., 2017; Borgonovo, Censi, et al., 2013; Grassi et al., 2015; Payer et al., 2013; Spies, Balmer, et al., 2015). A mean 2-year survival rate of 97.2% (CI 94.7–99.7) and a moderate degree of heterogeneity (I^2 = 58.0%, p = 0.036) was estimated (Figure 4). In addition, the meta-regression showed that the confounding factors did not have any significant effect on the survival rates (p > 0.05, Figure 5).

3.3 | Peri-implant marginal bone loss

Fourteen studies investigating 839 zirconia implants and 558 patients reported detailed marginal bone loss evaluations between implant placement and follow-ups (Table 3). Two studies had to be excluded from the 1-year MBL analysis as only panoramic radiographs were evaluated (Roehling et al., 2016) or detailed MBL values were only provided after 2 years of investigation (Mellinghoff, Cacaci, & Detsch, 2015). Thus, 12 studies evaluating periapical radiographs could be included in the 1-year meta-analysis (Figure 6).

3.3.1 | NCA zirconia implants

Data from 251 implants and 273 patients were available. The meta-analysis evaluation estimated a mean 1-year marginal bone loss

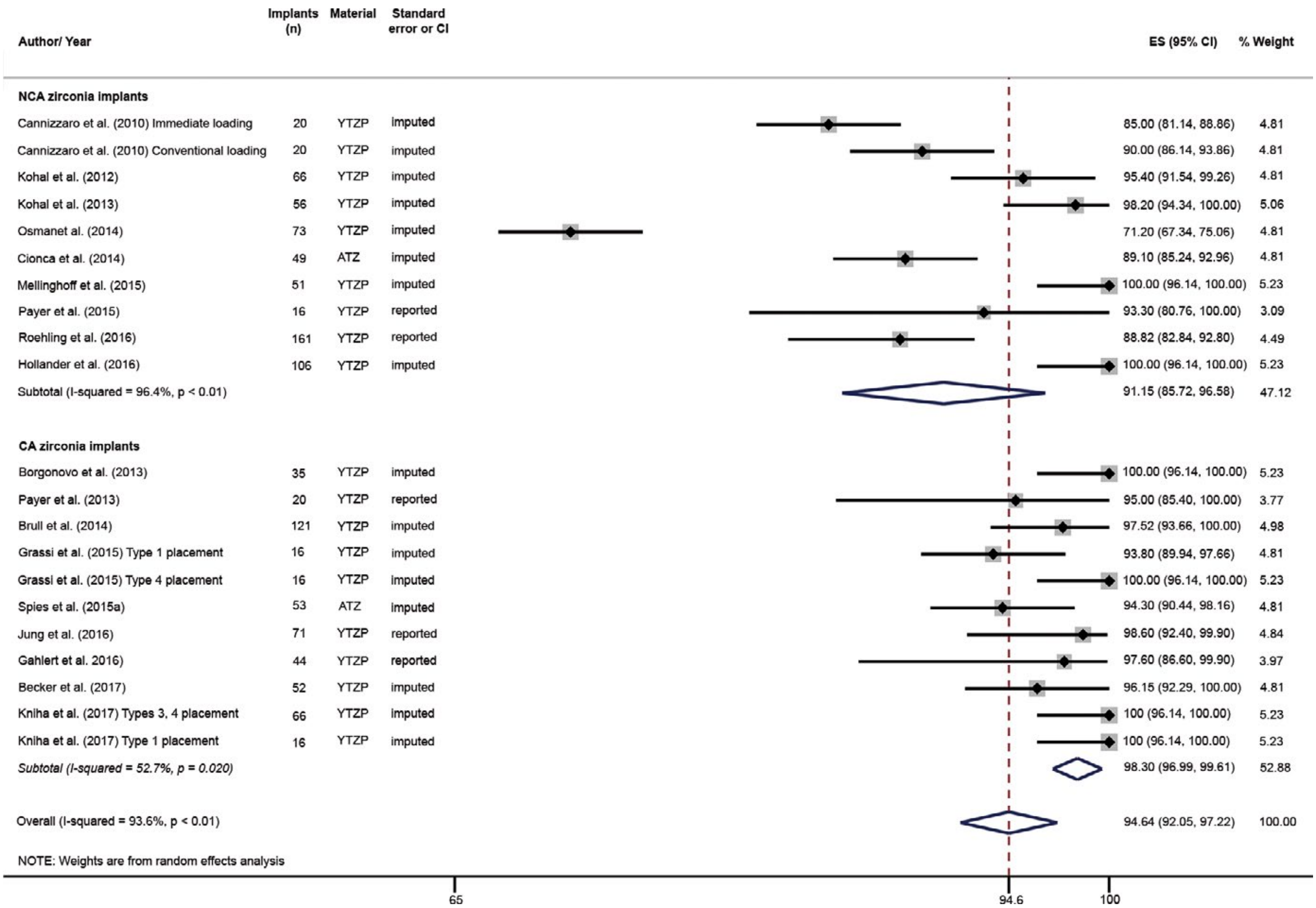

FIGURE 2 Forest plot of 1-year survival of NCA and CA zirconia implants. Significantly increased survival rates for CA compared with NCA zirconia implants (p = 0.028)

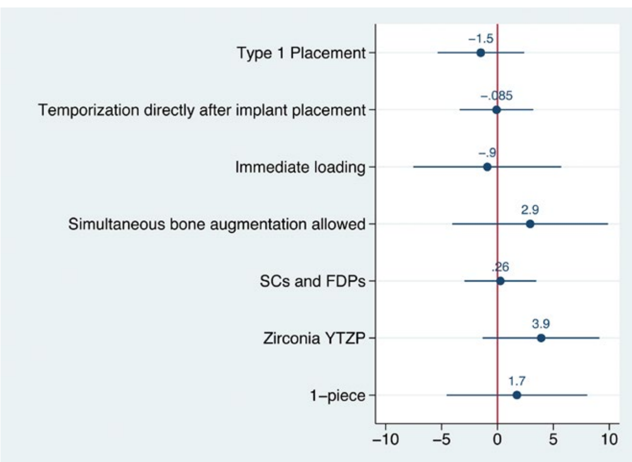

FIGURE 3 Effects of single factors on 1-year survival of CA zirconia implants. Illustrated are the estimated coefficients, including 95% confidence intervals. Coefficients >0 imply a positive effect on survival and coefficients <0 a negative effect on survival. All single 95% confidence intervals crossing the zero line imply no significant effect on implant survival

of 1.0 mm (CI 0.6–1.3). A high degree of heterogeneity was noted across the studies (I^2 = 93.2%, p < 0.01, Figure 6).

3.3.2 | CA zirconia implants

Overall, data from 376 implants and 285 patients were available. The evaluated mean 1-year marginal bone loss was 0.7 mm (CI 0.4–1.0). Again, a high degree of heterogeneity was found between the studies (I^2 = 95.9%, p < 0.01, Figure 6). The difference between NCA and CA zirconia implants was statistically not significant (p = 0.28).

The meta-regression for CA zirconia implants revealed that the type of implant placement, simultaneous bone augmentation procedures during implant placement, zirconia implant material and implant design did not have any significant effect on MBL (p > 0.05, Figure 5). Interestingly, temporization directly after implant placement and immediate implant loading were associated with increased MBL. However, these differences were not statistically significant (p > 0.05, Figure 7).

3.4 | Technical complications

Only 5 of 18 included studies investigating 263 implants (140 × NCA zirconia implants, 123 × CA zirconia implants) after follow-up periods between 12 and 24 months provided information with regard to technical complications or prosthetic outcomes, excluding implant fractures (Becker et al., 2017; Cannizzaro et al., 2010; Cionca et al., 2015; Jung et al., 2016; Mellinghoff et al., 2015). Taking both

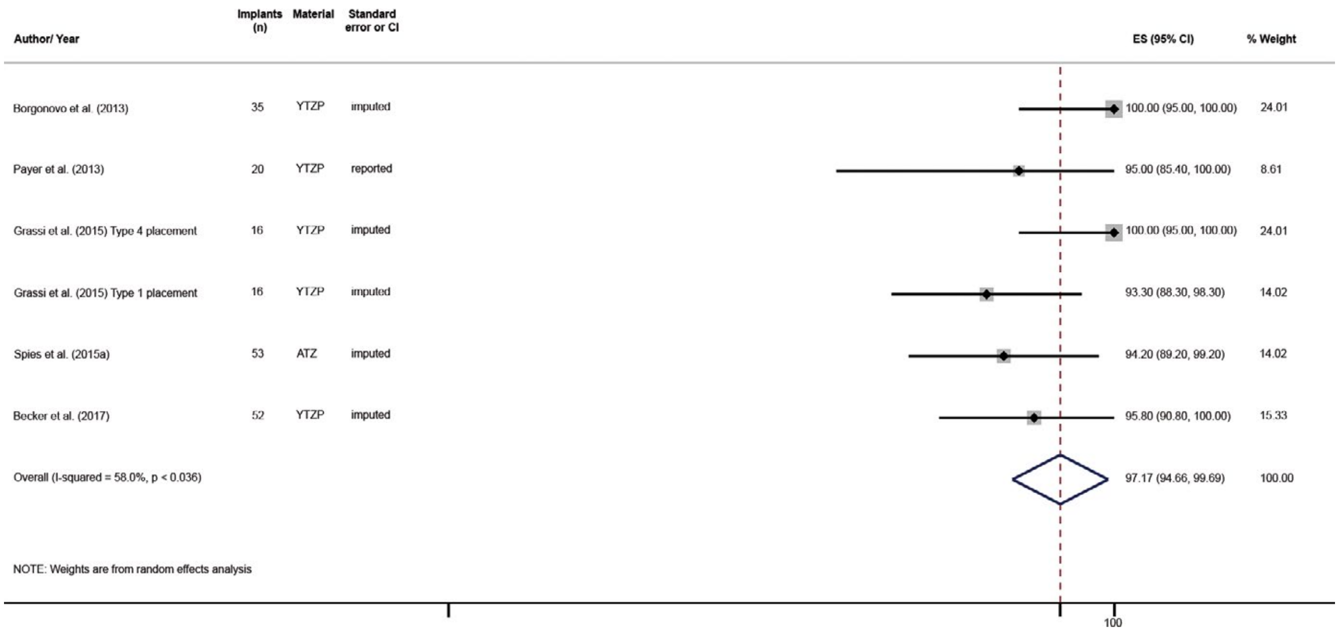

FIGURE 4 Forest plot of the 2-year survival of CA zirconia implants

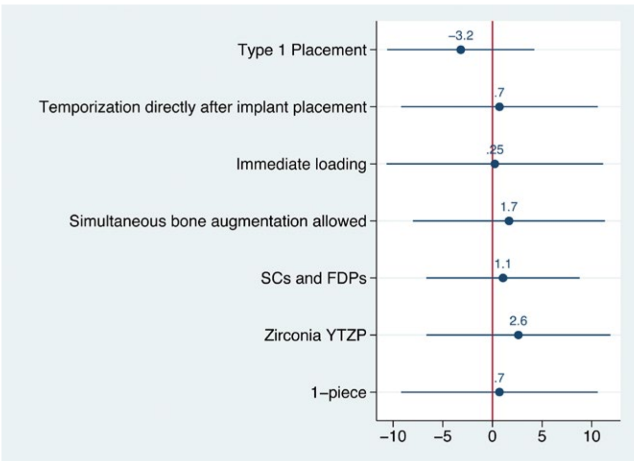

FIGURE 5 Effects of single factors on the 2-year survival of CA zirconia implants. Illustrated are the estimated coefficients, including 95% confidence intervals. Coefficients >0 imply a positive effect on survival and coefficients <0 a negative effect on survival. All single 95% confidence intervals crossing the zero line imply no significant effect on implant survival

types of implant generations together (NCA and CA zirconia implants), an overall complication rate of 3.4% was evaluated.

3.4.1 | NCA zirconia implants

When technical complications were observed for 1-piece zirconia implants restored with cement-retained SCs, the authors reported chipping of the veneering ceramic, fractures of the cemented crowns (4 SCs, 2.9%) or decementation (1 SC, 0.7% (Cannizzaro et al., 2010; Mellinghoff et al., 2015)). Moreover, when 2-piece zirconia implants were evaluated, 2 ATZ abutment fractures (1.4%) were observed during the functional loading period after cementation of the abutments and SCs. However, abutment fractures were not associated with zirconia implant fractures (Cionca et al., 2015). The overall technical complication rate for NCA zirconia implants was 5%.

3.4.2 | CA zirconia implants

Technical complications (1 SC chipping, fracture of the ceramic crown, 0.8%) were only reported for 2-piece zirconia implants restored with cement-retained SCs. In the same study, 1 fiberglass abutment fracture (0.8%) was observed during the loading period after cementation of the abutment and SC. Again, abutment fractures were not associated with implant fractures (Becker et al., 2017). Thus, an overall technical complication rate of 1.6% was evaluated for CA zirconia implants.

3.5 | Zirconia implant fractures

Three studies reported a total of 22 zirconia implant fractures (1.95%) in 16 patients (Tables 1 and 3).

3.5.1 | NCA zirconia implants

Twenty-one of 618 implants fractured (3.40%). Most of the fractures were observed in 1 study. In detail, Roehling et al. (2016) investigated 161 1-piece zirconia implants with different diameters after a mean follow-up of 5.9 years. The authors reported 18 fractures in 12 patients who occurred after a mean period of 15.3 months after placement. Of these 18 fractures, 15 implants had a diameter of 3.25 mm and only 3 implants had a diameter of 4.0 mm. Eleven implants were prosthetically restored with cement-retained SCs and 7 with cement-retained FDPs. Fourteen fractures were recorded in the maxilla and only 4 in the mandible. Moreover, Osman et al. (2014)

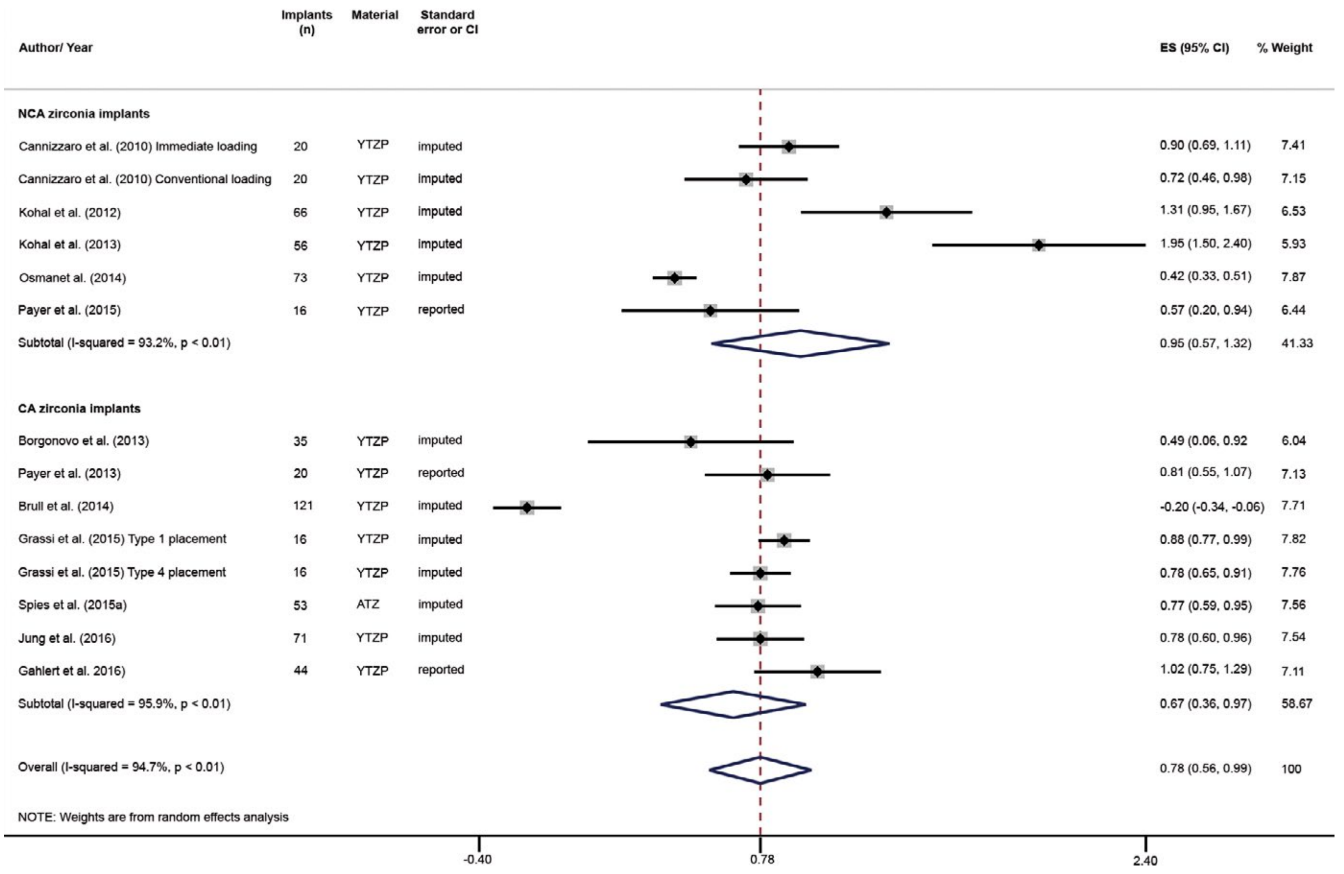

FIGURE 6 Forest plot of 1-year marginal bone loss of NCA and CA zirconia implants. No significant differences between NCA and CA zirconia implants

observed three 1-piece zirconia implant fractures in 3 patients who were restored with RHDs. Two implant fractures occurred in the maxilla and 1 in the mandible. No further information was provided with regard to the fracture details.

3.5.2 | CA zirconia implants

One of 510 zirconia implants fractured (0.20%). However, no information with regard to implant design, diameter, location and time point of implant fracture was reported (Brull et al., 2014).

3.6 | Biological complications

Overall, clinical and radiographic data from 1117 implants (689 × NCA zirconia implants, 428 × CA zirconia implants) were considered (Table 4).

3.6.1 | NCA zirconia implants

One study observed hypertrophic gingiva at 4 months after implant placement approximately 1 of 40 1-piece zirconia implants restored with cement-retained SCs (Cannizzaro et al., 2010). In addition, 2 studies investigating 1-piece zirconia implants evaluated marginal bone loss of more than 2 mm within the first year after

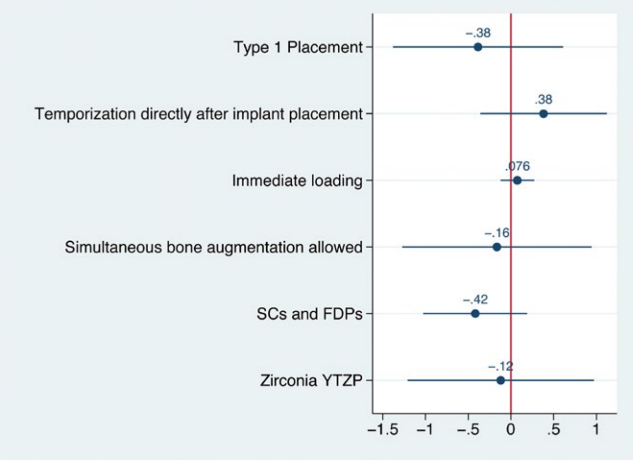

FIGURE 7 Effects of single factors on 1-year MBL of CA zirconia implants. Illustrated are the estimated coefficients, including 95% confidence intervals. Coefficients >0 imply an increase in MBL and coefficients <0 a decrease in MBL. All single 95% confidence intervals crossing the zero line imply no significant effect on MBL

implant placement for 41% and 39% of the investigated implants restored with cement-retained SCs and FDPs, respectively (Kohal et al., 2012, 2013). Overall, the incidence of biological complications was 7.3%.

3.6.2 | CA zirconia implants

One study reported "initial peri-implantitis" between 12 and 24 months after implant placement approximately 18 (37.5%) of 48 investigated 2-piece zirconia implants restored with cement-retained SCs. However, MBL analyses were not provided (Becker et al., 2017). Thus, an overall incidence of 4.2% was evaluated for biological complications.

3.7 | Aesthetic outcomes

Soft tissue outcomes were evaluated for 1- as well as for 2-piece zirconia implants restored with cement-retained SCs.

3.7.1 | NCA zirconia implants

A prospective RCT investigated 2-piece implants and directly compared titanium implants (restored with titanium abutments and ceramic crowns) to zirconia implants (restored with zirconia abutments and ceramic crowns). At baseline, after 6, 12, 18 and 24 months after crown cementation, PES scores of 2.4, 6.5, 9.0, 8.1 and 10.8, respectively, were reported for titanium. In contrast, zirconia implants showed significantly increased PES values of 6.9, 8.0, 10.3, 11.0 and 11.2 at corresponding time points (Payer et al., 2015). Another study observed that 69.8% of the placed 1-piece zirconia implants showed papilla scores of 2 and 3 according to Jemt after a mean follow-up period of 14.25 months (Hollander et al., 2016).

3.7.2 | CA zirconia implants

A prospective observational study investigated twenty 1-piece zirconia implants. PES scores of 8.1, 9.0 and 10.0 were reported at crown cementation, 12 and 24 months after implant placement. However, this increase was not statistically significant (Payer et al., 2013). When using the papilla index according to Jemt, a significant increase in papilla growth within the course of the investigation has been reported for 1-piece zirconia implants. In detail, only 17% of the papillae revealed indices of 2 and 3 at crown cementation, whereas 3 years after implant placement, this distribution significantly increased up to 56% (Spies, Balmer, et al., 2015).

4 | DISCUSSION

Implant survival was evaluated as one of the primary outcomes. Regarding NCA zirconia implants, the reported survival rates widely ranged between 71.2% and 100%, whereas the estimated mean 1-year survival rate was 91.15% (Table 4, Figure 2). Studies evaluating low overall survival rates of less than 80% observed high early implant failure and fracture rates (Osman et al., 2014; Roehling et al., 2016). CA zirconia implants showed less variation with regard to the reported survival rates (93.3%–100%) and a statistically significantly increased estimated mean 1-year survival rate (98.3%) compared with NCA zirconia implants ($p = 0.028$). In detail, more early and late failures as well as a higher implant fracture rate was evaluated for NCA (5.8% early failures, 2.6% late failures, 3.4% fractures) compared with CA implants (1.6% early failures, 0.6% late failures, 0.2% fractures). Interestingly, comparable values were reported for both generations of zirconia implants with regard to the reported quantitative surface characteristics (NCA: Ra: 0.5–5 μm; Sa: 1.24 μm; CA: Ra: 0.9–7.0 μm, Sa: 0.7–1.17 μm, Table 2). Consequently, the significantly improved survival rates might not just be attributed to increased quantitative surface roughness characteristics, but mainly to the 17 times higher fracture incidence for NCA zirconia implants compared with CA zirconia implants. However, it must be noticed that a comparison of single surface roughness parameters reported in different studies is not reasonable as standards and techniques for the used surface metrologies vary, and a successful osseointegration is not exclusively linked to one particular surface roughness feature (Jarmar et al., 2008; Wennerberg & Albrektsson, 2010). In addition to quantitative surface roughness, the morphological micro-textures and the surface treatment procedures are of high relevance for the osseous integration of zirconia implants, as experimental studies have reported that sandblasted and acid-etched zirconia implants with a surface roughness of 0.6 μm show similar bone-to-implant contact and removal torque out values compared with sandblasted and acid-etched titanium implants with a surface roughness of 1.2 μm (Bormann et al., 2012; Gahlert et al., 2009; Gahlert, Burtscher, et al., 2012; Gahlert, Roehling, et al., 2012).

When detailed information regarding early and late implant failures was provided, the authors reported that the suddenly noted implant mobility was not accompanied by any clinical signs of infection for cement-retained SCs on 2-piece implants (Cionca et al., 2015) and for cement-retained SCs and FDPs on 1-piece implants (Kohal et al., 2012, 2013; Roehling et al., 2016). Cionca et al., 2015 described these observations as "aseptic loosening", a term that was initially used in orthopedic total hip replacement surgery. The authors of the latter studies concluded that not bacterial infections but rather disintegration or premature loading may have caused the implant failures (Cionca et al., 2015; Kohal et al., 2012, 2013; Roehling et al., 2016). These findings are in contrast to results obtained for titanium implants showing that the main reasons for early implant failure were peri-implant inflammation, followed by failure of osseointegration (Han, Kim, & Han, 2014). The presently evaluated mean 1- and 2-year survival rates of 98.30% and 97.2%, respectively, for CA zirconia implants are comparable to data reported in systematic reviews on titanium implants, describing mean 1-year survival rates ranging from 96.8% to 99.5% (Benic, Mir-Mari, & Hammerle, 2014; Chambrone, Shibli, Mercurio, Cardoso, & Preshaw, 2015; Karl & Albrektsson, 2017). Previously, meta-analyses investigating zirconia implants reported 1-year survival rates of 92% (Hashim et al., 2016) and 95.6% (Pieralli et al., 2017), which are inferior compared with the presently evaluated survival rates for CA zirconia implants. However, both latter reviews evaluated overall survival rates that combined NCA and CA zirconia implants.

Based on the clinical relevance and significant impact on implant survival, the influence of confounding factors on primary outcomes using meta-regressions was evaluated only for CA zirconia implants. Immediate and conventional loading as well as early and late placement of zirconia implants showed reliable clinical outcomes within follow-up periods up to 2 years. However, immediate implant loading and type 1 implant placement tended to be associated with a non-significant decrease in implant survival (Figures 3 and 5). In addition to that, increased survival rates were calculated for 1- compared with 2-piece and for YTZP compared with ATZ zirconia implants. Again, the effects on survival rates were not statistically significant (Figures 3 and 5). It should be noted that these results also might have been influenced by the inclusion in the present review of only 2 studies investigating 2-piece zirconia implant systems and only 1 study evaluating ATZ implants (Table 1).

As an additional primary outcome, MBL was analyzed. The meta-analysis estimated a decreased mean 1-year MBL for CA (0.67 mm) compared with NCA zirconia implants (0.95 mm), but this difference was not statistically significant. Interestingly, all 2-piece zirconia implant systems that were included in the present review had a tissue level design. In this context, it must be noted that MBL is not only dependent on surface roughness or implant design (Hermann, Buser, Schenk, & Cochran, 2000; Valderrama et al., 2011) but also on surgical trauma during implant placement (Cochran et al., 1996) or the position of the rough/smooth border of 1-piece implants; in contrast, a subcrestal implant shoulder position leads to increased crestal bone loss (Hartman & Cochran, 2004; Hermann, Cochran, Nummikoski, & Buser, 1997; Hermann et al., 2011).

The mean 1-year MBL for CA zirconia implants (0.67 mm) is in agreement with previously published pooled data on NCA and CA zirconia implants after 1 year of investigation (0.79 mm, CI 0.73–0.86, (Pieralli et al., 2017)) and comparable to titanium implants after follow-up periods from 1 to 5 years (range 0.41–0.89 mm, (Karl & Albrektsson, 2017)). The meta-regression analysis for CA zirconia implants showed that none of the confounding factors had any significant effect on MBL (Figure 5). Based on the observation that only 1 publication provided pooled MBL values for 1- and 2-piece zirconia implants (Brull et al., 2014), implant design (1-piece compared with 2-piece macro design) could not be considered in the meta-regression evaluation for MBL.

In the present review, technical complications and implant fractures were considered as separate factors as only a few publications reported technical complications (Becker et al., 2017; Cannizzaro et al., 2010; Cionca et al., 2015; Jung et al., 2016; Mellinghoff et al., 2015), whereas information with regard to implant fractures was available for all included studies (Tables 3 and 4). The fracture incidence of NCA zirconia implants was clearly associated with a decreasing implant diameter (Roehling et al., 2016). Experimental investigations have shown that zirconia implants have the ability to withstand the forces of the oral cavity (Andreiotelli, Kohal, et al., 2009; Silva et al., 2009). However, uncontrolled surface treatment procedures like conventional sandblasting or uncontrolled machining or grinding processes can lead to surface micro-cracks and might reduce the fracture strength and lead to implant fractures in NCA 1-piece zirconia dental implants (Gahlert, Burtscher, et al., 2012; Osman, Ma, et al., 2013). Thus, manufacturing as well as uncontrolled grinding processes or a reduced implant diameter of NCA zirconia implants might have promoted the implant fractures reported in the present review. The presently evaluated fracture rate of 0.2% for CA zirconia implants is comparable to data reported in a systematic review on titanium implants, describing a mean titanium implant fracture rate of 0.2% after 5 years (Jung, Zembic, Pjetursson, Zwahlen, & Thoma, 2012).

With respect to biological complications, 2 studies investigating 1-piece NCA zirconia implants evaluated marginal bone loss of more than 2 mm within the first year after implant placement (Table 4). Interestingly, the authors of the latter studies reported that the increased MBL was not caused by inflammatory reactions to plaque or bacteria, but possibly were caused by the implant design or cement remnants in the peri-implant soft tissues (Kohal et al., 2012, 2013). Regarding CA zirconia implants, peri-implant infections were reported in 1 study and described as “initial peri-implantitis”, whereas longitudinal MBL data were not provided. Interestingly, the authors observed only “minor crestal bone levels not exceeding the upper 25% of the implant length” and only “moderate” probing depth values for the respective implants (Becker et al., 2017). Thus, a more pronounced physiological marginal bone level remodeling influenced by the implant design or surgical trauma during implant placement and not bacterial infection/peri-implantitis might rather be considered as a reason for the reported findings. The presently evaluated biological complication incidence of 4.2% for CA zirconia implants is comparable to data reported in systematic reviews on titanium implants for observation periods from 1 to 5 years (range 5.2%–7.1%, (Jung et al., 2012; Karl & Albrektsson, 2017; Zembic, Kim, Zwahlen, & Kelly, 2014)).

As a limiting factor of the present review, it should be noted that a wide range of quality of the reported clinical data was noted among the included studies. Thus, not every clinical relevant parameter could be extrapolated for analysis in the present review (e. g., implant diameter, implant location, type of implant placement, bone augmentation procedures, type of prosthetic reconstruction, prosthetic outcomes). In addition, the reported mean observation periods ranged from 12.00 to 71.28 months (5.94 years). Due to the wide variation regarding the follow-up periods, only 1-year meta-analyses and meta-regressions could be evaluated with regard to the primary outcomes when all included studies were considered. Thus, for the evaluation of the 2-years meta-analyses and meta-regressions, studies with observation periods of only 12 months had to be excluded. Based on the available clinical data, a statement concerning the clinical performance of zirconia compared with titanium implants is not possible as only 2 RCTs directly compared NCA zirconia to titanium implants (Osman et al., 2014; Payer et al., 2015). Moreover, the results of the present review showed that the available clinical data for zirconia implants can be confusing as different generations of zirconia implants have been scientifically investigated since the early 2000s. The market availability of zirconia implant generations should be considered when interpreting results from evidence-based investigations, a feature that becomes even more relevant since clinical studies and even meta-analysis published between 2016 and 2017 report outcomes for NCA zirconia implants (Hashim et al., 2016; Hollander et al., 2016; Pieralli et al., 2017; Roehling et al., 2016).

5 | CONCLUSIONS

Since the beginning of the 2000s, the clinical performance of CA zirconia implants has significantly improved compared with NCA implants. Regarding CA 1-piece zirconia implants, the present meta-analysis evaluated similar 1- and 2-years mean survival rates and peri-implant marginal bone loss after 1 year compared with published data on established titanium implants. Currently, CA 1-piece zirconia implants can be considered as a reliable treatment option for follow-up periods up to 2 years. Regarding the clinical application of 2-piece zirconia implants, very little evidence-based data are available. However, further prospective clinical long-term studies providing detailed information with regard to the time point of implant placement, type of loading, implant failures, biological and technical complications and prosthetic and aesthetic outcomes are urgently needed to confirm the present promising short-term findings.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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