

# Clinical Outcomes of Zirconia Dental Implants: A Systematic Review

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## Abstract

To determine the survival rate and marginal bone loss (MBL) of zirconia dental implants restored with single crowns or fixed dental prostheses. An electronic search was conducted up to November 2015 (without any restriction regarding the publication time) through the databases MEDLINE (PubMed), Cochrane Library, and EMBASE to identify randomized controlled clinical trials and prospective clinical trials including >15 patients. Primary outcomes were survival rate and MBL. Furthermore, the influence of several covariates on MBL was evaluated. Qualitative assessment and statistical analyses were performed. This review was conducted according to preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines for systematic reviews. With the applied search strategy, 4,196 titles could be identified. After a screening procedure, 2 randomized controlled clinical trials and 7 prospective clinical trials remained for analyses. In these trials, a total of 326 patients received 398 implants. The follow-up ranged from 12 to 60 mo. Implant loss was mostly reported within the first year, especially within the healing period. Thereafter, nearly constant survival curves could be observed. Therefore, separate meta-analyses were performed for the first and subsequent years, resulting in an implant survival rate of 95.6% (95% confidence interval: 93.3% to 97.9%) after 12 mo and, thereafter, an expected decrease of 0.05% per year (0.25% after 5 y). Additionally, a meta-analysis was conducted for the mean MBL after 12 mo, resulting in 0.79 mm (95% confidence interval: 0.73 to 0.86 mm). Implant bulk material and design, restoration type, and the application of minor augmentation procedures during surgery, as well as the modes of temporization and loading, had no statistically significant influence on MBL. The short-term cumulative survival rates and the MBL of zirconia implants in the presented systematic review are promising. However, additional data are still needed to confirm the long-term predictability of these implants.

**Keywords:** ceramics, zirconium dioxide, bone resorption, meta-analysis, osseointegration, implant supported dental prosthesis

## Introduction

Oral implants have represented an important improvement in patients' care for 4 decades (Brånemark et al. 1977). The gold standard materials for the fabrication of oral implants are commercially pure titanium or its alloys, with expected survival rates of 93% to 95% after 10 y when supporting fixed restorations (Jung et al. 2012; Pjetursson et al. 2012). Apart from the well-documented benefits of titanium as implant material, its disadvantages are represented by potential discoloration of the peri-implant soft tissue (Thoma et al. 2016), possible hypersensitivity (Hosoki et al. 2016), and the debated contribution to peri-implantitis development (Fretwurst et al. 2016). With the introduction of titanium implants, alumina implants ( $\text{Al}_2\text{O}_3$ ) have been commercialized (Sandhaus 1968). Unfortunately, the clinical performance of those ceramic implants was poorly documented. Alumina implants are no longer available, apparently because of their high risk of fracture (Andreietelli et al. 2009). Meanwhile, an alternative oxide ceramic material has been introduced. Zirconia (zirconium dioxide [ $\text{ZrO}_2$ ]) presents the phenomenon of allotropy, allowing for a phase transformation toughening mechanism. This results in improved mechanical properties as increased fracture strength and toughness (Garvie et al. 1975). Mostly used as yttria-stabilized tetragonal zirconia polycrystal (Y-TZP), this material has the potential to represent a valid alternative to titanium for the manufacturing of oral

implants. Preclinical studies on 1-piece zirconia implants addressing their fracture resistance exhibited promising results for their clinical use. Furthermore, in vitro studies proved the biological positive response of osteoblasts and osteoblast-like cells in regard to attachment and proliferation with results similar to titanium (Bächle et al. 2007). Several in vivo studies demonstrated a high biocompatibility of zirconia implants and an excellent degree of osseointegration (Akagawa et al. 1993; Kohal et al. 2004). As for titanium implants, roughened surfaces seem to be beneficial for this purpose (Manzano et al.

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A supplemental appendix to this article is published electronically only at <http://jdr.sagepub.com/supplemental>.

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2014). The first clinical studies of 1-piece zirconia oral implants were presented in 2006 (Blaschke and Volz 2006; Mellinghoff 2006). However, initial studies were retrospective or included a limited pool of patients. Since 2010, several prospective clinical trials evaluating implant survival and marginal bone loss (MBL) have been performed. The majority of these studies were conducted with 1-piece implants, while just a few considered newly developed 2-piece implants (Becker et al. 2015; Payer et al. 2015). The most recently published systematic review of clinical investigations analyzed the survival and success rate of zirconia implants (Hashim et al. 2016). However, a mixture of indications (fixed, removable) and implant designs (e.g., root analogue) was included. This resulted in a lack of implications for clinical practice and further research. Furthermore, MBL was not statistically evaluated. To the present day, several newly published prospective investigations with up to 5 y of follow-up (Grassi et al. 2015; Jung et al. 2015; Spies, Balmer, et al. 2015) have not been included in any systematic review.

Therefore, the aim of this review was to systematically collect randomized controlled clinical trials (RCTs) and prospective clinical studies available in the literature on zirconia implants restored with fixed prostheses and statistically analyze their behavior in relation to survival rate and MBL. Additional parameters were evaluated, including implant design (1 piece / 2 piece), temporization mode (immediate/delayed), loading mode (immediate/delayed), bulk material, and the influence of minor augmentation procedures.

## Materials and Methods

This systematic review was conducted following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (Moher et al. 2009) and the patient, intervention, comparison, outcomes (PICO) method (Scharadt et al. 2007) as applicable in relation to the topic of the review:

*Patient:* Partially edentulous patients

*Intervention:* Rehabilitation with zirconia implants

*Comparison:* Titanium implants

*Outcomes:* Survival rate, MBL

### Focused Question

In terms of implant survival and MBL, how reliable are zirconia dental implants restored with single crowns (SCs) and fixed dental prostheses (FDPs)?

### Information Sources and Data Extraction

The electronic search was performed with the databases MEDLINE (PubMed), Cochrane Library, and EMBASE with a platform-specific search strategy consisting of combinations of controlled terms (MeSH/EMTREE) and text words. No restrictions regarding the type of study were applied, but a language limitation to articles written in English, German, Italian, and Spanish language was performed. In addition, a manual search was conducted to screen the references of the included

publications for relevant articles. Two reviewers (S.P., B.C.S.) independently conducted the electronic and manual search, and any disagreement was resolved by discussion with a third author (R.J.K.).

### Screening Process

The search strategy used for MEDLINE/PubMed was a combination of MeSH and text words without any filters:

*(((dental implants[MeSH Terms]) AND ceramics[MeSH Terms])) OR ((dental implantation[MeSH Terms]) AND ceramics[MeSH Terms])) OR (((zirc\*) OR tzp\*) OR atz\*)) AND (((implant) OR implants) OR implantation) OR implanted))*

The search strategy for EMBASE was a combination of EMTREE and text words:

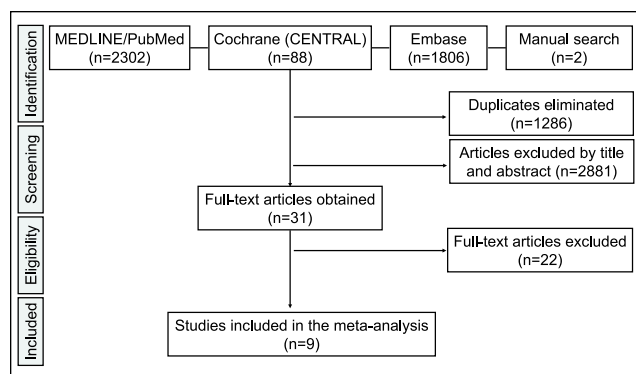
*(((CT=dental implants) AND CT=ceramics)) OR (((CT=dental implantation) AND CT=ceramics)) OR (((zirc\*) OR tzp\*) OR atz\*)) AND (((implant) OR implants) OR implantation) OR implanted))*

Finally, the search performed in the Cochrane Library database is available in the appendixes (Fig. 1).

The search was performed on November 2, 2015, for all mentioned databases. There was no lower limit for the analyzed time frame. Obtained publications were imported into reference management software (EndNote X6; Thomson Reuter) and subsequently screened.

### Eligibility Criteria

To achieve a higher level of evidence (at least level III according to the U.S. Agency for Health Care Policy and Research published in 1993; Appendix Table 1), this review was limited to RCTs and prospective clinical trials that mentioned the survival rate and the MBL of zirconia implants that were restored with SCs or 3-unit FDPs. Furthermore, at least 15 patients per study were required as a supplementary inclusion criterion. Two authors (S.P. and B.C.S.) independently eliminated any duplicate from the gathered results and examined the remaining articles by title and abstract. Subsequently, the full texts were obtained and analyzed for further inclusion/exclusion. In addition, the authors of relevant articles were contacted per email and asked for any further information, if necessary. Both reviewers extracted the data from the included full-text studies, and any disagreement was resolved by consensus. Reviewers' agreement was statistically evaluated through the Cohen's kappa test. Further eligible data considered were number of patients/implants at the beginning of the study and at the last follow-up, patients' mean age, types of restorations (SCs and FDPs), mean observation period (months) of the implants, implant survival rate (percentage), MBL (millimeter), temporization mode (immediate/delayed), loading mode (immediate/delayed), use of augmentation procedures during surgery (yes/no), implant design (1 piece / 2 piece), and implant bulk material (Y-TZP / alumina-toughened zirconia [ATZ]).



**Figure 1.** Flowchart of study selection according to the PRISMA guidelines.

### Risk of Bias

To reduce the risk of bias, this review was designed according to the PRISMA checklist and flow diagram. Furthermore, the AMSTAR checklist (A Measurement Tool to Assess Systematic Reviews) was followed, if applicable.

### Qualitative Assessment

The quality assessment was conducted through the Cochrane Collaboration's tool for assessing risk of bias for the evaluation of the RCTs. In addition, the Newcastle-Ottawa Scale was utilized for the analysis of the nonrandomized cohorts. Two reviewers (S.P. and B.C.S.) independently evaluated the included studies. The agreement between the authors was evaluated with the Cohen's kappa test.

### Statistical Analyses

For the MBL after 12 mo, a meta-analysis was performed. To take a potential clustering effect within patients into account, computation of study-specific standard errors was based on the average number of patients and average number of implants. Metaregression was used to examine the effect of several covariates (as mentioned above) on MBL. For the survival rates, 2 separate meta-analyses were used, as decreasing survival curves could be observed in the first 12 mo and nearly constant curves afterward. In the first analysis, all reported 1-y survival rates were included. In the second analysis, the available survival rates for those implants that survived the first year were computed. The study-specific standard errors of both survival rates were computed combining the averaged observed survival rates and the study-specific number of implants/patients. Forest plots were used for graphic presentation.

## Results

### Screening Process

The initial search yielded 4,198 articles, of which 1,286 were duplicates. After exclusion of the duplicates as well as

publications irrelevant to the topic of this systematic review, 31 articles remained. Of these 31 articles, a full-text analysis was performed; thereafter, a further 22 articles could not be included in the final analysis. These publications were excluded for  $\geq 1$  of the following reasons: 1) they were designed as retrospective trials; 2) they did not mention the implant MBL; or 3) they considered  $<15$  patients (Fig. 1).

The screening process resulted in a total of 9 articles that could be included in the present systematic review (Table 1). Of these, 2 were randomized controlled clinical trials, whereas 7 were prospective cohort clinical investigations. All included studies were published within the last 6 y, 5 of them not until 2015 (Grassi et al. 2015; Jung et al. 2015; Payer et al. 2015; Spies, Balmer, et al. 2015; Gahlert et al. 2016). All selected articles reported on either single- or multiple-teeth replacement with implant-supported SCs or FDPs. The calculation of the Cohen's kappa coefficient proved an interrater agreement of 0.98%. The reasons for exclusion for the 22 articles that were not considered for statistical analyses can be found in Table 2.

### Quality Assessment

RCTs were analyzed with the Cochrane Collaboration's tool for assessing risk of bias (Appendix Table 2). Both RCTs provided sufficient data regarding the sequence generation, allocation concealment, and outcome reporting. However, the study of Payer and colleagues (2015) revealed a potential attrition bias. Furthermore, a possible performance bias could be found in both RCTs, mostly owing to impossible blinding of the clinician and the incomplete blinding of the outcome assessor in the study of Cannizzaro et al. (2010). Industrial support represented a questionable font of bias in both cases. The qualitative assessment of the included prospective clinical trials was conducted with the Newcastle-Ottawa Scale for cohort investigations (Appendix Table 3) and resulted in a valuation with 7 stars in most cases. Only 6 stars could be assigned to the investigation of Payer et al. (2013) due to the low follow-up rate ( $<80\%$ ), accompanied by an insufficient description of lost patients/implants. Finally, the study of Spies, Balmer, et al. (2015) received an additional star in the category of comparability for furnishing sufficient data on the peri-implant soft tissue parameters of adjacent teeth. The resulting Cohen's kappa coefficient was 0.91%.

### Demographic and Implant Data

The 9 studies included a total of 326 patients with a mean patient age ranging from 38 to 57.2 y (Table 1). A total of 398 implants were inserted with a follow-up between 12 mo (Cannizzaro et al. 2010; Gahlert et al. 2016) and 60 mo (Grassi et al. 2015). Studies that included both types of restorations (SCs/FDPs; Jung et al. 2015; Spies, Balmer, et al. 2015) or different loading concepts (immediate/delayed; Cannizzaro et al. 2010) were split and evaluated independently. As a result, 294 implants restored with SCs and 104 implants restored with FDPs were evaluated.

**Table 1.** Results of the Included and Analyzed Articles.

	Pts, n	Mean Age, y	Imp, n	Mean Obs Per, mo	12 mo <sup>a</sup>		Immediate			Implant	
					Survival, %	Mean $\pm$ SD MBL, mm	Temp	Load	SAA	D/P	Bulk
Cannizzaro et al. (2010) <sup>b</sup>	20	39	20	12	90 (—)	0.72 $\pm$ 0.59 (—)	x		x	1	Y
Cannizzaro et al. (2010) <sup>c</sup>	20	38	20	12	85.0 (—)	0.9 $\pm$ 0.48 (—)	x	x	x	1	Y
Payer et al. (2013)	20	44.4	20	17.1	95 (95)	0.81 $\pm$ 1 (1.29 $\pm$ 0.1)	x			1	Y
Payer et al. (2015)	12	46	16	19.7	93.3 (93.3)	1.16 $\pm$ 1.01 (1.48 $\pm$ 1.05)				2	Y
Kohal et al. (2012)	65	39.3	66	36.9 <sup>f</sup>	95.5 (90.8) <sup>f</sup>	1.31 $\pm$ 1.49 (—)	x		x	1	Y
Kohal et al. (2013)	28	53.6	56	36.9 <sup>f</sup>	98.2 (98.2) <sup>f</sup>	1.95 $\pm$ 1.71 (—)	x		x	1	Y
Gahlert et al. (2016)	44	48	44	12.5	97.6 (—)	1.02 $\pm$ 0.9 (—)			x	1	Y
Spies, Balmer, et al. (2015) <sup>d</sup>	27	44.4	27	36.8	88.9 (88.5)	0.46 $\pm$ 0.54 (0.47 $\pm$ 0.49)	x		x	1	A
Spies, Balmer, et al. (2015) <sup>e</sup>	13	57.2	26	37.1	100 (100)	1.08 $\pm$ 0.67 (1.07 $\pm$ 0.68)	x		x	1	A
Jung et al. (2015) <sup>d</sup>	49	47.1	49	34.8 <sup>f</sup>	97.9 (97.7) <sup>f</sup>	0.66 $\pm$ 0.61 (—)	x		x	1	Y
Jung et al. (2015) <sup>e</sup>	11	54.1	22	36.5 <sup>f</sup>	100 (100) <sup>f</sup>	0.44 $\pm$ 0.42 (—)	x		x	1	Y
Grassi et al. (2015)	17	52.3	32	61.2	96.9 (96.8)	0.83 $\pm$ 0.24 (1.23 $\pm$ 0.29)	x	x	x	1	Y

A, alumina-toughened zirconia; Bulk, bulk material; D/P, design/pieces; Imp, implants; Load, loading; MBL, marginal bone loss; Obs Per, observation period; Pts, patients; SAA, simultaneous augmentation allowed; Temp, temporization; x, procedures were done; Y, yttria-stabilized tetragonal zirconia polycrystal.

<sup>a</sup>Value in parentheses indicates end of follow-up.

<sup>b</sup>No immediate loading.

<sup>c</sup>Immediate loading.

<sup>d</sup>Single crowns.

<sup>e</sup>Fixed dental prostheses.

<sup>f</sup>Unpublished data.

**Table 2.** Reasons for Exclusion When 31 Full-Text Articles Were Screened.

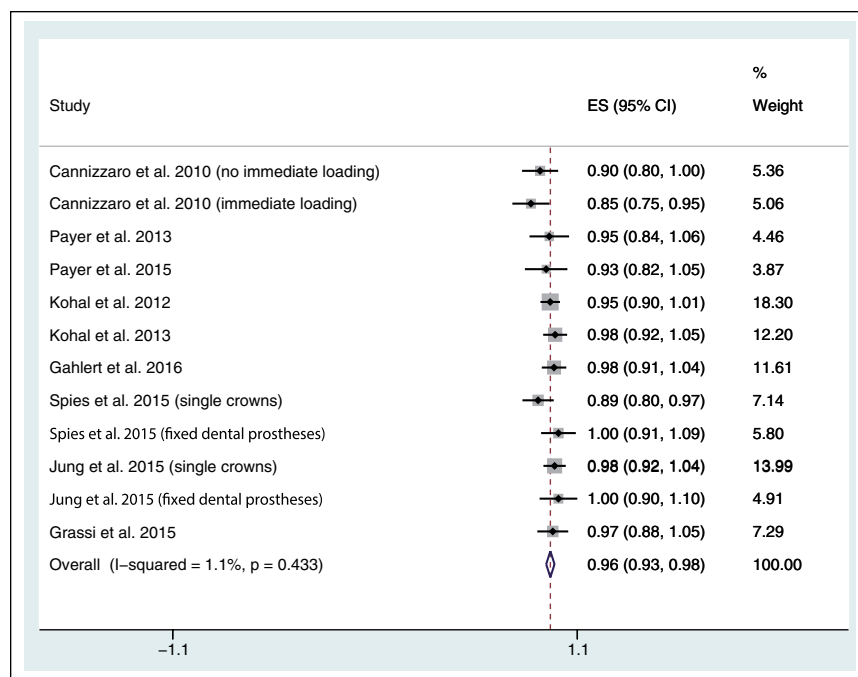
Article	Reason for Exclusion
Bankoğlu Gungor et al. (2014)	<15 patients
Becker et al. (2015)	No MBL measurements
Blaschke and Volz (2006)	No MBL measurements, retrospective design
Borgonovo et al. (2010)	No MBL measurements, retrospective design
Borgonovo et al. (2011)	No value for mean MBL provided
Borgonovo et al. (2012)	<15 patients
Borgonovo, Censi, et al. (2013)	<15 patients
Borgonovo, Corrocher, et al. (2013)	<15 patients
Borgonovo, Vavassori, et al. (2013)	<15 patients
Borgonovo et al. (2015)	<15 patients, no MBL measurements
Brüll et al. (2014)	Retrospective design
Cionca et al. (2015)	No value for mean MBL provided
Gahlert et al. (2013)	Retrospective design
Kollar et al. (2008)	No zirconia implants
Lambrich and Iglhaut (2008)	No MBL measurements, retrospective design
Mellinghoff (2006)	No MBL measurements, retrospective design
Oliva et al. (2007)	No MBL measurements, retrospective design
Oliva et al. (2010)	No MBL measurements
Pirker and Kocher (2008)	Case report
Pirker and Kocher (2009)	<15 patients, no MBL measurements
Roehling et al. (2015)	Retrospective design
Spies, Sperlich, et al. (2016)	Same cohort in Spies, Balmer, et al. (2015)

MBL, marginal bone loss.

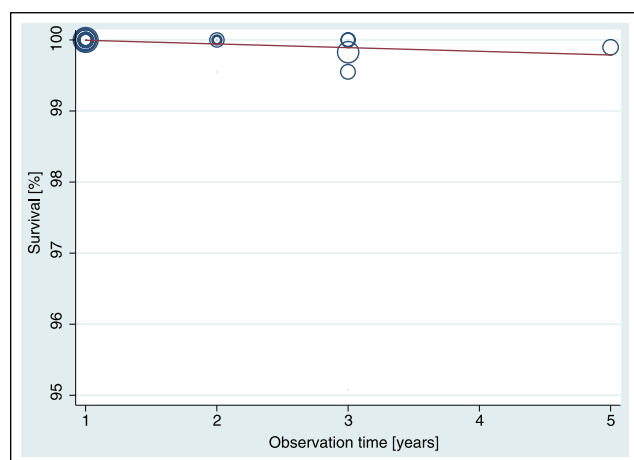
## Implant Survival

Of the 398 implants placed, 347 were examined to the last follow-up (Fig. 2). The survival rate after 12 mo ranged between 85% (Cannizzaro et al. 2010) and 100% (Jung et al. 2015; Spies, Balmer, et al. 2015). According to the different outcomes of the studies, our meta-analysis resulted in a 1-y

implant survival rate of 95.6% (95% confidence interval [95% CI]: 93.3% to 97.9%). Based on the available data exceeding 1 y of observation, an expected decrease of 0.05% per year afterward was calculated (Fig. 3). Most implant failures occurred in the early period after placement (Cannizzaro et al. 2010; Kohal et al. 2012; Payer et al. 2013; Grassi et al. 2015; Jung et al. 2015; Spies, Balmer, et al. 2015).



**Figure 2.** Forest plot of the survival rate after 12 mo. 95% CI, 95% confidence interval; ES, effect size.



**Figure 3.** Ongoing survival of implants surviving the first 12 mo.

### Marginal Bone Loss

The MBL was evaluated at certain follow-ups and measured on standardized radiographs (Fig. 4). The MBL values after 12 mo ranged between 0.44 mm (SD: 0.42 mm; Jung et al. 2015) and 1.95 mm (SD: 1.71 mm; Kohal et al. 2013). The meta-analysis of the 12-mo data resulted in an MBL of 0.79 mm (95% CI: 0.73 to 0.86 mm). Any further meta-analysis of the MBL could not be performed due to the lack of long-term data.

### Type of Restorations

Of the included studies, 6 solely addressed single-tooth replacements (Cannizzaro et al. 2010; Kohal et al. 2012; Payer et al.

2013; Grassi et al. 2015; Payer et al. 2015; Gahlert et al. 2016), whereas only 1 study solely considered multiple lost teeth rehabilitated with 3-unit FDPs (Kohal et al. 2013). Finally, 2 studies included both indication types (Jung et al. 2015; Spies, Balmer, et al. 2015) and were therefore split into 2 independent cohorts according to the type of restoration (SC or FDP) and analyzed separately. No statistically significant difference regarding MBL could be observed for SCs (0.80 mm) and FDPs (0.76 mm) with the applied meta-analysis ( $P = 0.455$ ).

### Implant Temporization

In 7 studies, immediate temporization was performed. Six of these studies described the immediate temporization of the implants with provisional acrylic restorations (Cannizzaro et al. 2010; Kohal et al. 2012; Kohal et al. 2013; Grassi et al. 2015; Jung et al. 2015; Spies, Balmer, et al. 2015). In the seventh study (Payer et al.

2013), the implants were immediately restored with all-ceramic CAD/CAM provisionals without occlusal contacts, and after a healing period of 4 mo, the implants were restored with all-ceramic crowns. Finally, in 2 of the included studies, a delayed-temporization concept was preferred. In 1 study (Gahlert et al. 2016), the provisional restorations were delivered 11 to 13 wk after implant placement. In a second investigation (Payer et al. 2015), abutment connection with a 2-piece implant took place 4 to 6 mo after implant placement. The meta-analysis did not show a statistically significant difference in MBL (immediate: 0.79 mm, delayed: 1.05 mm;  $P \geq 0.546$ ) when evaluating for an effect of the temporization mode.

### Implant Loading

In 1 study (Cannizzaro et al. 2010), patients were randomly rehabilitated with either an immediately or nonimmediately loaded prosthesis. The failure rate between the 2 groups was not statistically significant. An immediate loading concept was also applied in the investigation of Grassi et al. (2015). Five other studies used a nonimmediate occlusal loading concept for the rehabilitation of the implants, placing the provisionals out of occlusion. The meta-analysis showed no statistically significant influence regarding MBL (immediate: 0.84 mm, non-immediate: 0.75 mm;  $P \geq 0.985$ ) when evaluating for an effect of the loading mode.

### Bone Regeneration

Only 2 studies did not allow any type of bone augmentation technique during implant placement (Payer et al. 2013; Payer et al. 2015). One investigation included major augmentations at least 3 mo before implant placement (Gahlert et al. 2016).

Six studies stated that “minor bone augmentation” procedures (Cannizzaro et al. 2010; Gahlert et al. 2016) were applied during surgery. Grassi et al. (2015) described the augmentation procedures as synthetic bone grafts, while other studies (Jung et al. 2015; Kohal et al. 2012; Kohal et al. 2013; Spies, Balmer, et al. 2015) referred to guided bone regeneration procedures with autogenous bone or bovine bone covered with a resorbable membrane. No statistically significant difference could be calculated regarding MBL ( $P \geq 0.815$ ) between applied augmentation procedures (0.79 mm) and no augmentation procedure during surgery (0.97 mm).

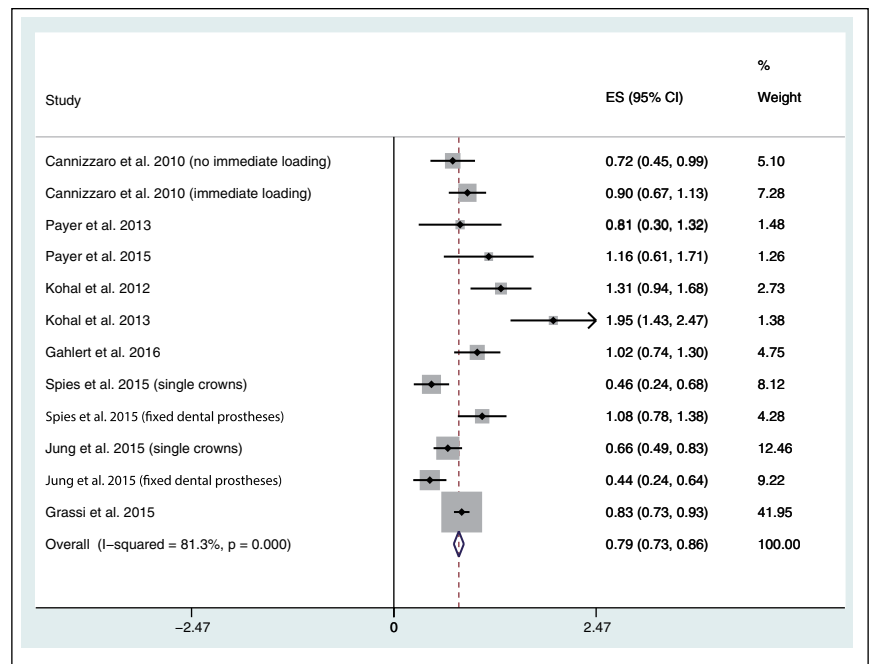
### Implant Design and Implant Bulk Material

One of the 9 included studies evaluated a 2-piece implant system (Payer et al. 2015), whereas the others installed a 1-piece implant. No statistically significant difference was observed regarding MBL (1 piece: 0.79 mm, 2 piece: 1.16 mm;  $P = 0.586$ ). In 1 study (Spies, Balmer, et al. 2015), the bulk material of the implants consisted of ATZ, while the other 8 studies were conducted with implants made from Y-TZP. No statistically significant difference was found regarding MBL (ATZ: 0.67 mm, Y-TZP: 0.81 mm;  $P = 0.565$ ).

## Discussion

### Reported Survival Rates

Relating to the primary outcome, survival rates were used to analyze the clinical performance of the evaluated implants. The parameter survival was mainly defined as an implant remaining in situ irrespective of modifications during the observation period. The statistical analysis of the present review included the presently available data and, furthermore, the unpublished survival rates of 3 ongoing studies performed by the authors of this review (Kohal et al. 2012; Kohal et al. 2013; Jung et al. 2015). The meta-analysis resulted in a survival rate of 95.6% after 12 mo. This can be considered comparable to titanium implants likewise supporting SCs and FDPs (Jung et al. 2012; Pjetursson et al. 2012). Nevertheless, the cohorts of 2 included studies showed reduced survival rates of 85% (Cannizzaro et al. 2010) and 88.9% (Spies, Balmer, et al. 2015). Cannizzaro et al. (2010) reported that all immediately loaded implants installed in extraction sites were lost. Data for immediately restored implants placed in fresh extraction sockets are still rare and a topic of controversial discussion in the literature. Chaushu et al. (2001) could show that immediately placed and immediately



**Figure 4.** Forest plot of marginal bone loss after 12 mo. 95% CI, 95% confidence interval; ES, effect size.

restored 2-piece titanium implants resulted in a lower survival rate when compared with nonimmediately placed and immediately temporized implants. Similarly, Esposito et al. (2015) referred to fewer complications with delayed implant placement versus immediate postextractive implants. Moreover, Cristalli et al. (2015) advised that selection of patients and a rigorous clinical protocol are fundamental for postextraction implant placement and loading. Therefore, immediate restoration of immediately placed implants might result in reduced survival rates, irrespective of the implant material. A second cohort with a reduced survival rate was found in the study of Spies, Balmer, et al. (2015), where a new tapered implant design was investigated. The authors reported that the first 3 implants placed did not osseointegrate, whereas all subsequently installed implants remained in situ at the 3-y follow-up. They concluded that a certain learning curve might be necessary on how to handle 1-piece implants. Finally, the short-term survival rates from the included studies showed positive results and might therefore be considered promising.

### Applied Success Criteria/MBL

Due to the heterogeneity of the applied success criteria in the included studies (Albrektsson et al. 1986; Buser et al. 1990; Naert et al. 1992; Östman et al. 2007), any comparisons of the reported success rates would not be appropriate. As clearly shown in the investigations of Kohal and colleagues (Kohal et al. 2012; Kohal et al. 2013), the evaluation of marginal bone level changes might be the most important criterion for the assessment of success of dental implants. In their investigations, survival rates as high as 95.4% and 98.2% could be observed

after 1 y. However, when we consider MBL as a success criterion, only 66% and 62% of the implants could be assigned to success grade I ( $\leq 2$  mm of MBL) and 86% and 87% to success grade II ( $\leq 3$  mm of MBL; Östman et al. 2007). Therefore, the evaluation of marginal bone-level changes was considered mandatory for inclusion in the present review. According to the conclusions stated at the consensus report of the proceedings of the First European Workshop on Periodontology, an MBL of  $<1.5$  mm after 1 y of functional loading and 0.2 mm annually thereafter might be defined a successful treatment outcome. The meta-analysis conducted in our systematic review resulted in an MBL of 0.79 mm after 12 mo, which might be considered a successful outcome after 1 y. Furthermore, no covariates were found to significantly affect MBL. Thus, the MBL of zirconia implants can be considered similar to the ones reported for titanium implants. However, due to the heterogeneity of the included studies and some controversial results, more data are necessary for final evaluation of this topic.

### *Suitability of the Search Strategy*

Limiting the database search to combinations of MeSH terms is a common procedure (Jung et al. 2012; Pjetursson et al. 2012). For the electronic search strategy of the present review, a combination of MeSH terms and text words was utilized to enhance the sensibility of the search and minimize the risk of inadvertent exclusion of relevant articles. Processing of newly published articles in MEDLINE takes a considerable amount of time. Therefore, a strategy limited to MeSH terms might result in a loss of relevant data. For example, no MeSH terms had been assigned to 4 included studies in November 2015. Consequently, we recommend combining different specific MeSH terms with various combinations of adequate text words.

### *Implant Bulk Materials and Surface Treatments*

Regarding the implant bulk material, the majority of the included studies involved implants produced from Y-TZP, whereas only 1 study investigated newly developed ATZ implants coated with Y-TZP (Spies, Balmer, et al. 2015). However, implants exclusively produced from ATZ are market available. ATZ is an oxide ceramic composite material with increased fracture strength and reduced aging susceptibility (Kohorst et al. 2012; Spies, Sauter, et al. 2015; Spies, Nold, et al. 2016). To date, no clinical studies including implants exclusively made of ATZ can be found in the literature. However, there is some evidence from preclinical animal studies (Schierano et al. 2015; Kohal et al. 2016) suggesting an osseointegration capability comparable to Y-TZP.

### *Soft Tissue Parameters*

Because of the lack of (Cannizzaro et al. 2010) and the heterogeneity of the presented data, no statistical evaluation of the

soft tissue parameters could be performed. Soft tissue measurements were predominantly performed at each follow-up and described as secondary outcomes after survival rate and MBL. Various parameters were screened, although mostly through different measurements methods (e.g., bleeding on probing, probing depth, clinical attachment loss, bleeding indices, plaque indices, gingival recessions, and papilla height). In addition to the peri-implant evaluations, the adjacent teeth were frequently taken as references. In 1 investigation, only a “healthy soft tissue” (Jung et al. 2015) in the peri-implant area was described, whereas others found decreased bleeding and plaque indices in the course of the follow-ups (Kohal et al. 2012; Kohal et al. 2013; Payer et al. 2013). However, significantly different results in relation to reference teeth were described for probing depth and other parameters (Kohal et al. 2012; Kohal et al. 2013). Moreover, comparison of parameters across studies revealed heterogeneous outcomes. For statistical analyses, standardized and identical soft tissue evaluations would have been necessary.

### *Limits and Risk of Bias of the Review*

It has to be mentioned that the principal limits of the present review can be found in the lack of high-quality controlled clinical trials and the short-term follow-up of most of the included studies. In regard to the main risk of bias, an industrial involvement was found for all mentioned investigations. Apart from the above-mentioned limits, we prepared this review in respect of the presently available and recommended guidelines.

### *Implications for Clinical Practice and Further Research*

For restoring single-tooth gaps and replacing up to 3 adjacent missing teeth, zirconia implants can be considered a treatment option with an outcome comparable to titanium implants. There are no sufficient data available addressing extended indications. Based on the performed analyses, the time point of temporization and loading has no influence on MBL, thereby indicating no need for protective splints during the healing period. Although 1-piece implants do not allow for primary wound closure, minor augmentation procedures during implant installation showed no significant effect on MBL. However, especially for unexperienced surgeons and prosthodontists, correct placement of 1-piece implants and immediate temporization might be a challenging demand. Furthermore, patient selection is considered a crucial point for this indication. This might explain the calculated failure rate of 4.4% within the early healing period and suggest a learning curve even for experienced dentists, as described by Spies, Balmer, et al. (2015). However, implants surviving the first year can be considered at low risk of failure (0.05% per year). To overcome the limitations of 1-piece implants, further research should address the long-term stability of 2-piece zirconia implants before evaluating their reliability clinically.



## Conclusion

An increasing interest for zirconia and its composites as dental implant materials has been shown in the last few years, as testified by numerous clinical studies published on this topic. Based on the present systematic review, the survival rate and MBL of zirconia dental implants supporting SCs and FDPs after 1 y are promising and, furthermore, comparable to available data of 2-piece titanium implants. However, more high evidence-level clinical studies are needed to confirm the long-term predictability of these implants.

## Summary

Dental implants made of zirconia have been commercially available for several years. Besides numerous promising pre-clinical investigations, an increasing number of clinical investigations were recently published, especially in 2015. Therefore, the aim of this review was to systematically analyze the behavior of zirconia oral implants restored with fixed restorations in relation to survival rate and marginal bone. Furthermore, the eventual influence of many covariates was evaluated. The design of this review followed the PRISMA guidelines, the AMSTAR checklist, and the PICO method. A comprehensive search through the main databases (MEDLINE/PubMed, Cochrane Library, and EMBASE) and text references was performed up to November 2015. The inclusion criteria were defined as follows: 1) fixed restoration (SCs or 3-unit fixed dental prostheses), 2) calculation of survival rate, 3) calculation of mean MBL, 4) prospective study design, and 5) minimum of 15 included patients. From the initial screening, a total of 4,198 articles were obtained; furthermore, the full text of 31 articles was extracted. Thereafter, 22 full-text articles were excluded, and 9 studies were finally included in this review (5 of them published in 2015). Additionally, unpublished data of 3 included studies were obtained (3 y of follow-up). For the meta-analysis, the data sets were split in relation to the type of restoration and independently analyzed. Two separate meta-analyses were conducted in relation to the survival rate after 12 mo and the further follow-ups. In addition, a meta-analysis was performed to evaluate the mean MBL after 12 mo and the eventual influence of several covariates on it. To assess the quality of the included studies, the most recommended rating scales were used: the Cochrane Collaboration's tool for assessing risk of bias for RCTs and the Newcastle-Ottawa Scale for the nonrandomized investigations. According to our meta-analysis, the survival rate after 1 y was of 95.6% (95% CI: 93.3% to 97.9%) with a further decrease of 0.05% per year afterward (0.25% after 5 y). Furthermore, the statistical evaluation of the peri-implant MBL resulted in 0.79 mm (95% CI: 0.73 to 0.86 mm) with no statistically significant influence from any of the evaluated parameters. From our point of view, a 12-mo survival in the range of 95% without significant decrease afterward and a calculated amount of MBL <1 mm can be considered highly successful.

## Author Contribution

S. Pieralli, contributed to the design of the review, data acquisition, data interpretation and analysis and wrote the manuscript; R.J. Kohal, contributed to the design of the review, data acquisition and interpretation and critically revised the manuscript; R.E. Jung, contributed to data analysis and critically revised the manuscript; K. Vach, performed the statistical analysis and critically revised the manuscript; B.C. Spies, contributed to the design of the review, data acquisition, data interpretation and critically revised the manuscript. All authors gave final approval and agree to be accountable to all aspects of the work.

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