Is Zirconia a Viable Alternative to Titanium for Dental Implantology?

Keywords

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ABSTRACT

Aim: To review the literature using a systematic approach to answer the question: 'Are zirconia dental implants an alternative to titanium dental implants?' This was evaluated by assessing the evidence for survival rate, success rate and marginal bone loss of the two implant materials. Methods: Relevant studies were identified after searching PUBMED, EMBASE and the Cochrane library. Two reviewers assessed the papers using the specified inclusion criteria, title and abstracts. Studies that were not related to the outcomes of: survival rate, success rate or marginal bone loss of zirconia dental implants were excluded. Results: From a total of 1617 titles and abstracts, 33 potentially relevant full text papers were identified. Of these, 18 met the criteria for inclusion in the review. The review revealed heterogeneity between the studies in terms of surgical characteristics, implant characteristics, defining success and measuring marginal bone loss therefore making comparisons between studies difficult. However, in the three randomised control studies included in this review, which compared zirconia implants to titanium implants, the survival rate was lower for zirconia implants, but the success rate and marginal bone loss were found to be similar. Conclusion: Overall, initial studies indicate that zirconia dental implants could be a viable alternative to titanium implants but need further well-designed studies need to be carried out to assess their long-term survival rate, success rate and marginal bone loss. At present, zirconia implants should be used with caution but can be an alternative option if a patient has an absolute contraindication to titanium.

INTRODUCTION

Many general dental practitioners are placing dental implants for patients as part of their rehabilitation plan. More than 1300 types of dental implants are available, in different materials, shapes, sizes, lengths and surface characteristics.[1]

Most titanium dental implants are made from Grade 4 commercially pure Titanium (cpTi), as it is stronger than the other grades.[2] Titanium can also be used as an alloy with Vanadium (V) and Aluminium (Al). These alloys increase the elastic modulus and the tensile strength of the implant while decreasing the chance of corrosion.[3] The properties of high strength, low modulus of elasticity, biocompatibility, corrosion resistance and ability to osseointegrate give titanium remarkable advantages over other materials for dental implants.[4]

Titanium's main disadvantage is the dark colour of the metal which changes the peri-implant tissue when measured by a spectrophotometer.[5] This is a major concern in the anterior region of the oral cavity where an unaesthetic greyish gingival margin can be seen in patients with a thin gingival biotype. A clinical study of 1500 dental implant patients showed a 0.6% prevalence

of titanium allergy.[6] Although inconclusive there are suggestions that some patients may develop an allergy to titanium through release of metal ions into the peri-implant tissue leading to allergic responses and sensitisation.[7,8,9] These limitations and an increase in the demand for aesthetic dentistry, due to the media, has increased patients' demands for more aesthetic and metal free restorations.[10] This has increased the popularity of all ceramic restorations in dentistry.

Zirconia exists in the three crystalline phases, Monoclinic, Cubic and Tetragonal depending on the temperature. The latter is the one that is used clinically. Yttrium is added to the Tetragonal to make it stable and it forms Yttria Tetragonal Zirconia Polycrystal (YTZP), which is the formulation used for zirconia dental implants.[11]

Zirconia has superior mechanical properties compared to titanium in terms of strength and hardness.[12] These properties prevent the deformation of zirconia under occlusal forces and cyclic stresses.[12,13] Many studies have found no local or systemic adverse reactions or cytotoxic effects to zirconia, demonstrating its biocompatibility with soft and hard tissues of the body, a major advantage over titanium.[12] *In vitro* and *in vivo* studies have shown that zirconia accumulates fewer bacteria than titanium.[14-16]

Survival is defined as an implant being present in the mouth independent of biological and/or technical complications.[17] The criteria to define success in implant dentistry are under constant debate in which different criteria take different factors into consideration. Albrektsson *et al.* (1986)[18] proposed criteria which considered bone loss, i.e. 'vertical bone loss be less than 0.2 mm annually after first year of the implant placement'.[18] Newer criteria devised by International Congress of Oral Implantologists (ICOI) considered the amount of crestal bone lost during the first year should be no more than 2mm.[19] Marginal bone loss (MBL) is a therefore a key consideration in the survival and success of a dental implant as it directly affects the stability of the implant. MBL also affects the gingival sulcus depth which leads to the gingival margin moving more apically and exposing the implant leading to poorer aesthetics.

Two systematic reviews have suggested zirconia dental implants should not be used routinely in clinical dentistry. The reason for this advice was at that time most clinical studies of zirconia dental implants were animal trials even though there was no difference in the rate of osseointegration in those studies.[20,21] A more recent systematic review concluded that zirconia implants exhibited a lower survival rate and higher MBL compared to titanium.[22] Another review concluded that the survival rate of zirconia implants was 95.6% after 12 months and there was an expected decrease of 0.05% per year and MBL of 0.79 mm after 12 months, which showed promising signs for the use zirconia dental implants when compared to the criteria mentioned above.[23]

It is evident from the literature that zirconia has many advantages over titanium as a dental implant biomaterial. However, there is conflicting evidence on survival rate, success rate and MBL for zirconia implants. Against this background, the aim of this study was to review the current literature using a systematic approach to answer the question: 'Are zirconia dental implants an alternative to titanium dental implants?' This was evaluated by assessing the evidence for survival rate, success rate and MBL of each implant material.

METHODS

SEARCH STRATEGY

The electronic databases PubMed, EMBASE and the Cochrane central register of controlled trials were used to search for studies.

A focussed clinical question was developed using the PICO (Patients, Intervention, Comparison, Outcome) method.[24] It was: when a partial or completely edentulous patient received a titanium or zirconia dental implant, did the implant material affect the survival rate, success rate and MBL?

The PubMed database was searched using several combinations of Medical Subject Heading (MeSH) terms and keywords were used in sequence with Boolean variables OR and AND:

- P: edentulous jaw, partial edentulous jaw, edentulous mouth, partial edentulous mouth
- I: dental implant, dental implantation, endosseous dental implant
- C: zirconia, zirconium dioxide, yttria-stabilised tetragonal zirconia polycrystal, ceramic implant
- O: success rate, survival rate, marginal bone loss, crestal bone loss

The Embase database was searched using several combinations of Emtree terms with Boolean variables as above.

In addition, implant and periodontal journals were searched manually. Finally, references of included and excluded studies were screened to find any relevant studies.

ELIGIBILITY CRITERIA

Studies were considered for this review if they met the following inclusion criteria:

- Ten or more human participants
- Written in English up to 30th April 2019
- Randomised controlled trials (RCT), non-randomised controlled studies, cohort studies, case control studies where the clinical outcomes of survival rate, success rate and MBL for zirconia dental implants were reported
- Twelve or more months of follow up

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Studies that did not meet these criteria were excluded from this review, including studies investigating alumina toughened zirconia implants.

As there were limited RCTs available on this topic, a systematic approach in the form of a rapid review, rather than a true systematic review was performed.[25]

DATA EXTRACTION

The data extraction process was carried out by two independent reviewers (HV and KE) using a data extraction form. The data extraction form was piloted on three studies to ensure the relevant data was captured and that there was no confusion between the reviewers with regard to its use.

There were several confounding variables that were considered for further evaluation which were included in the data extraction form as they can affect the reliability and validity of results obtained in this review:

- Study design
- Patient factors - systemic conditions, smoking, bruxism
- Implant design- surface treatment, surface roughness
- Surgical factors- timing of implant placement, bone augmentation, loading protocol
- Success criteria used
- MBL- radiograph used, reference point, sites measured, investigators

The timing of implant placement was classified according Hämmerle *et al.*[26] and the implant loading protocol was classified according to Weber *et al.*[27]

METHODOLOGICAL QUALITY ASSESSMENT

No systematic reviews were included due to the unavailability of true systematic reviews which only reviewed RCT's. The quality of evidence of the studies included in this review was graded according to the Oxford Centre for Evidence-Based Medicine (OCEBM) grading system and will be analysed and discussed in the discussion section of this review.

Any difference in opinion between the reviewers was discussed so that an agreement could be made. This ensured inter-reviewer reliability.

RESULTS

A search strategy generated an initial list of 1617 publications (*Figure 1*). By using the exclusion criteria, 1584 were excluded after analysis of titles and abstracts, leaving 33 potential articles for full text review agreed by two independent reviewers (HV and KE). The data extraction form was utilised for the 33 articles and after analysis 18 studies were chosen for the review. The other 15 publications were excluded. Justifications for their exclusion are presented in Table 1.

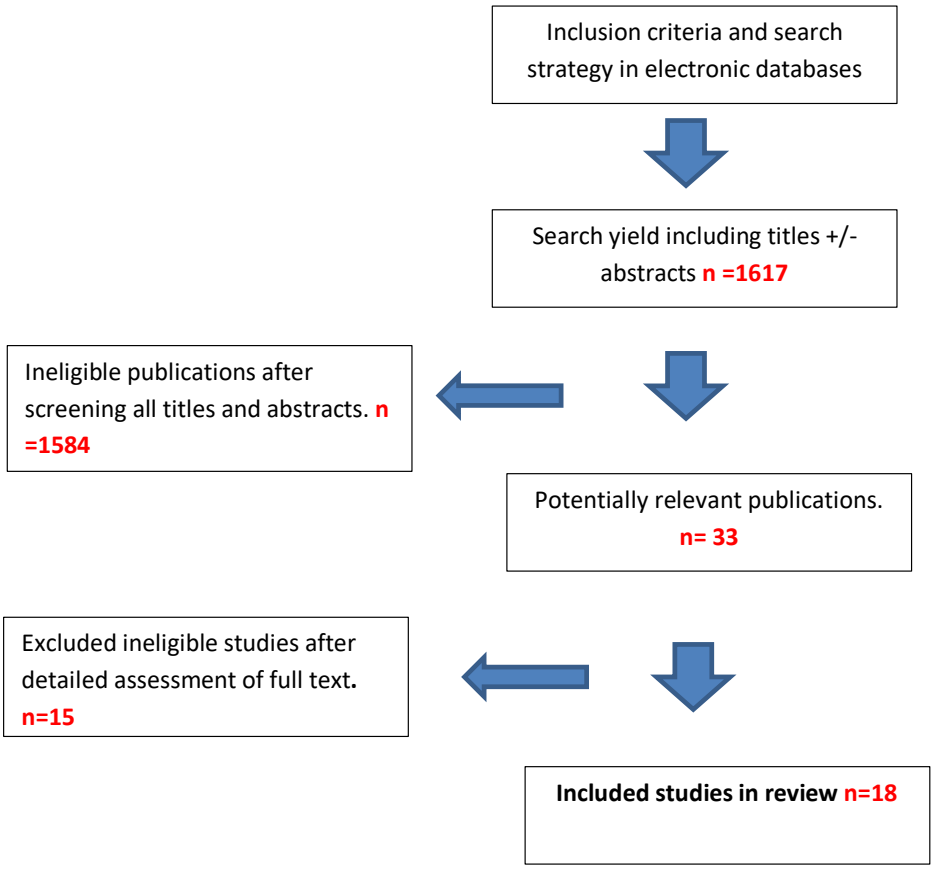

Figure 1: Flow diagram for data extraction

Table 1. Justifications for exclusion

Reason for exclusion	Study
Same sample of patients as in the included studies	Borgonovo *et al.* (2011), Borgonovo *et al.* (2015), Gahlert *et al.* (2013), Gahlert *et al.* (2015), Holländer *et al.* (2016), Jung *et al.* (2015), Kniha *et al.* (2018), Kniha *et al.* (2018) Kohal *et al.* (2012), Oliva *et al.* (2007), Osman *et al* (2014).[28-38]
Investigated Alumina Toughened Zirconia Implants	Cionca *et al.* (2014), Spies *et al.* (2015).[39,40]
Investigated individually designed root shape implants	Pirker *et al.* (2009).[41]
Investigated prosthetic outcome as the primary aim	Spies *et al.* (2017).[42]

PATIENT DEMOGRAPHICS

From Table 2 it can be seen all the studies were published in the last 10 years with majority from Europe. Eleven of the studies selected their sample of patients from prosthetic or maxillofacial departments of university hospitals. All of the patients in the studies were 18 years or older. The minimum follow-up period in the included studies was 12 months but one reported up to 93.6 months.[43]

All studies, except Brull *et al.*[44] study, excluded patients who had contraindications for implant surgery (e.g. immunodeficiency, advanced systematic disease, corticosteroid medication, pregnancy, previous irradiation to head/neck area). Eleven studies also specified the exclusion of diabetic patients from their studies.[43,45-53] Only nine studies documented exclusion of patients with active periodontitis or without proper periodontal maintenance care. Three studies excluded patients who smoked tobacco,[47,50,54] two did not mention the of exclusion of smokers[46,49] and the remaining studies included smokers.[43-45,48,51-53,55-60] Ten studies excluded patients who had parafunctional habits, for example bruxism.[43,45,47-49,51,53, 54,56,60,

Table 2 summarises the patient demographics in the selected studies.

IMPLANT CHARACTERISTICS

The number of Yttria-stabilised Tetragonal Zirconia Polycrystal (YTZP) implants placed in the sample varied from 16[47] to 831[55] with a cumulative total of 1840 zirconia implants placed in all 18 studies. The length of the YTZP implants varied from 6mm[57,58] to 16mm.[46,49] The diameter of the YTZP implants also varied from narrow 3.25mm[43,45] to 6mm.[58]

Table 3 summarises the implant characteristics of implants used in the selected studies.

SURGICAL CHARACTERISTICS

Eight of the studies included implants that were immediately placed after the tooth had been extracted as a one surgery procedure.[44-46,48-50,52,55] The timing of the implant placement in two of the studies was not mentioned.[43,56] The remaining of the studies waited a minimum of four to eight weeks for soft tissue coverage.[47,51,53,54,57-60]

Three studies did not carry out simultaneous bone augmentation.[46,49,58] One study did not record whether or not bone augmentation was carried out.[43] The remaining studies carried some degree of bone augmentation along with the implant placement.[44,45,47,48,50-57,59,60]

Three studies immediately loaded their implants with the final prosthesis.[48,54,60] Another three studies had a combination of immediate and conventional loading of implants.[45,52,55] The remaining studies waited at least two or more months to functionally load their implants.

Table 4 summarises the surgical characteristics of implants used in the selected studies.

SURVIVAL RATE AND SUCCESS RATE

The survival rate varied in the studies of zirconia implants from 71.2%[57] to 100%.[43,48,56] All three RCT's comparing titanium and zirconia showed lower survival rates for zirconia implants, 82.2% to 71.2% at 12 months,[57] 88.3% to 76.5% at 12 months,[58] 100% to 93.3% at 24 months.[47]

Ten studies recorded the success rate for the implants with eight studies not recording the success rate. The success rate for zirconia implants ranged from 67.6%[58] to 100%.[48,56]

One of the RCT recorded a lower success rate for zirconia implants compared titanium implants, 93.3% to 100% at 24 months.[47] Another RCT recorded a very minimal higher success rate for zirconia implants compared titanium implants, 67.6% to 66.7% at 12 months.[58]

One study did not record their success criteria[53] and the remaining nine studies followed various success criterion for dental implants as shown in table 5. Only five studies success criteria considered MBL.[48,50,55,56,58]

The Alberktsson *et al.*[18] criteria stated that a success rate of 85% at five years should be deemed successful. Only three studies were followed up for more than 60 months and out of the three studies only one showed more than 85% success rate at 93.3%,[48] one did not record success rate[43] and one was below 85% at 77.6%.[59] This presents varied results for the long-term success of zirconia implants.

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Table 2. Patient demographic of the included studies

Study Number	Author	Year	Country	Study Design	Level of evidence	Setting	Sample Size	Age range (years)	Mean Age (years)	Follow up (months)
1	Lorenz *et al.*	2019	Germany	PC	3	Uni	38	39-80	63.5	93.6
2	Bormann *et al.*	2018	Germany	PC	3	Uni+PP	44	18-78	48	36
3	Rodriguez *et al.*	2018	USA	R	4	PP	12	27-86	55	25
4	Balmer *et al.*	2017	Germany	PC	3	Uni	60	20-70	48.1	36
5	Becker *et al.*	2017	Germany	PC	3	Uni	60	18-80	47.6	24
6	Kniha *et al.*	2017	Germany	PC	3	Uni+PP	78	NR	55	12
7	Kohal *et al.*	2017	Germany	PC	3	Uni	65	18-70	NR	36
8	Grassi *et al.*	2015	Italy	PC	3	Uni+PP	17	35-70	52.3	61.2
9	Payer *et al.*	2015	Austria	RCT	3	Uni	22	24-77	46	24
10	Roehling *et al.*	2015	Switzerland	R	4	PP	85	19-85	54.9	71.3
11	Siddiqi *et al.*	2015	New Zealand	RCT	3	Uni	24	50-79	62	12
12	Brull *et al.*	2014	Netherlands	R	4	Uni	74	18-72	51	18.4
13	Osman *et al.*	2014	New Zealand	RCT	3	Uni	24	46-80	62	12
14	Borgonovo *et al.*	2013	Italy	P	4	Uni	13	38-75	60	48
15	Kohal *et al.*	2013	Germany	P	4	Uni	28	18-70	NR	12
16	Payer *et al.*	2013	Austria	P	4	Uni	20	27-71	44.4	24
17	Cannizzaro *et al.*	2010	Italy	RCT	3	PP	40	18-54	38	12
18	Olivia *et al.*	2010	Spain	P	4	NR	378	19-80	48.2	40.8

Key: P= prospective case series, R= retrospective case series, PC= prospective cohort study, RCT= randomised control trial, PP= private practice, Uni= university hospital, NR- not recorded

Tables 5 summarise the survival and success rate of implants used in the selected studies.

MARGINAL BONE LOSS

Four of the studies included in this review did not record the MBL.[50,51,55,58] From the 14 studies that recorded the MBL around zirconia implant, the MBL ranged from 0.3mm[52] to 1.95+- 1.71mm.[46]

Two studies measured the MBL using orthopantomograms (OPG)[43,59] and remaining studies used periapical (PA) radiographs and all measurements were made with computer software using digital radiographs.

Two studies did not mention the how many sites were measured for MBL.[49,60] The remaining twelve studies mentioned measuring the MBL at two sites (mesial and distal) on the radiographs.

Three studies did not mention their reference points for measuring MBL.[44,52,60] Six studies measured MBL from implant shoulder to crestal bone.[43,47,53,54,56,59] Three studies measured MBL from lower edge of implant abutment to most coronal visible point of bone-to-implant contact.[46,48,49] One study measured the MBL from apical margin of the implant collar to the most coronal visible point of bone-to-implant contact.[45] Another study measured MBL from top of the ball abutment to the most coronal visible point of bone-to-implant contact.[57]

All except one study Lorenz *et al.*[43] recorded their method of calibration using the known length, diameter, inter-thread of the implant.

Two studies used two independent investigators,[52,57] five studies used one independent investigator[46,47,49,53,54] and one study used a non-independent investigator to measure the MBL.[45] The remaining of the studies did not mention if the investigator measuring the MBL was independent or non-independent of the study.

One of the RCT's showed that zirconia implants had more MBL than titanium implant, 0.42+-0.4mm to 0.18+-0.47mm.[57] Another RCT showed similar MBL, 1.48 +-1.05 mm for zirconia and 1.43 +- 0.67 mm for titanium.[47]

Table 6 summarises the MBL of implants used in the selected studies.

Table 3. Implant characteristics of the included studies

Study Number	Reference	Number of implants	Material	Implant system	Surface treatment	Surface Roughness (µm)	Length (mm)	Diameter (mm)	Connection
1	Lorenz *et al.* 2019	83	YTZP	Z-Look 3 (Z systems)	SB	NR	8-14	3.25-5	1
2	Bormann *et al.* 2018	31	YTZP	Pure Ceramic (Strauman)	SB+AE	0.7	8-14	4.1	1
3	Rodriguez *et al.* 2018	24	YTZP	Z systems	NR	NR	NR	NR	1,2
4	Balmer *et al.* 2017	66	YTZP	Vita Zahnfabrik	SB+AE	1.2	8-14	4-5.5	1
5	Becker *et al.* 2017	48	YTZP	Zircon vision	SB	7	9-13	4.5-5	2
6	Kniha *et al.* 2017	82	YTZP	Pure Ceramic (Strauman)	SB+AE	0.7	8-12	4	1
7	Kohal *et al.* 2017	66	YTZP	Ziunite (nobel)	sintering	1.24	10-16	4.3-5	1
8	Grassi *et al.* 2015	32	YTZP	WhiteSky (bredent)	SB+MN	1.17	10-14	3.5-5.5	1
9	Payer *et al.* 2015	15	Ti	Ziterion vario T	SB	NR	11.5	4	2
		16	YTZP	Ziterion vario Z	SB	NR	10-13	4	2
10	Roehling *et al.* 2015	161	YTZP	Z-Look 3 (Z systems)	SB	NR	10-13	3.25-5	1
11	Siddiqi *et al.* 2015	48	Ti	Southern implants	SB+AE	1-2	6-11.5	3.8-5	1
		62	YTZP	Southern implants	SB+AE	0.5-0.8	6-11.6	3.8-6	1
12	Brull *et al.* 2014	121	YTZP	ZV3 Zircon vision	Sintering	7.0	8	3.5	1,2
13	Osman *et al.* 2014	73	YTZP	Southern implants	AE	1-2	6-11.5	3.8-5	1
		56	Ti	Southern implants	SB+AE	1-2	6-11.5	3.8-5	1
14	Borgonovo *et al.* 2013.	28	YTZP	WhiteSky (bredent)	SB+MN	0.9-1.0	10-14	4	1
15	Kohal *et al.* 2013	56	YTZP	Ziunite (nobel)	sintering	1.24	10-16	4.3-5	1
16	Payer *et al.* 2013	20	YTZP	WhiteSky (bredent)	SB	1.17	10-14	3.5-4.5	1
17	Cannizzaro *et al.* 2010	40	YTZP	Z-Look 3 (Z systems)	SB	NR	10-14	3.25-5	1
18	Olivia *et al.* 2010	831	YTZP	CeraRoot	UC,C,AE	0.92,1.16	NR	NR	1

Key: Ti= titanium, YTZP= yttria-stabilised tetragonal zirconia polycrystal, SB= sand blasted, AE= acid etched, MN= machine necked, UC= uncoated, C=coated, NR= not recorded

Table 4. Surgical characteristics of the included studies

Study Number	Reference	Implant timing	Bone augmentation	Implant loading protocol
1	Lorenz *et al.* 2019	NR	NR	Conventional
2	Bormann *et al.* 2018	2,3,4	Yes	Conventional
3	Rodriguez *et al.* 2018	1,2,3,4	Yes	Immediate/conventional
4	Balmer *et al.* 2017	2,3,4	Yes	Immediate
5	Becker *et al.* 2017	2,3,4	Yes	Conventional
6	Kniha *et al.* 2017	1,3,4	Yes	Conventional
7	Kohal *et al.* 2017	1,2,3,4	Yes	Conventional
8	Grassi *et al.* 2015	1,4	Yes	Immediate
9	Payer *et al.* 2015	4	No	Conventional
10	Roehling *et al.* 2015	2,3,4	Yes	Conventional
11	Siddiqi *et al.* 2015	3,4	No	Conventional
12	Brull *et al.* 2014	1,2,3,4	Yes	Conventional
13	Osman *et al.* 2014	4	Yes	Conventional
14	Borgonovo *et al.* 2013	NR	Yes	Conventional
15	Kohal *et al.* 2013	1,2,3,4	Yes	Conventional
16	Payer *et al.* 2013	3,4	No	Immediate
17	Cannizzaro *et al.* 2010	1,2,3,4	Yes	Immediate/conventional
18	Olivia *et al.* 2010	1,2,3,4	Yes	Immediate/conventional

Key: NR= not recorded

DISCUSSION

LIMITATIONS OF THE REVIEW

The key characteristics of a systematic review described by Chandler *et al.*[61] were all met by this review but there were some limitations.

During the data collection phase, the proposed search strategy had to be slightly amended. When a large number of the search terms were used together, it produced very little or no results due the limited literature available on zirconia implants. When used in smaller combinations, for example 'Zirconia' AND 'Dental implant' AND 'Survival rate' produced more studies, therefore this approach was utilised in order to retrieve more studies to be screened.

Unfortunately, at the time of the review there were only 3 RCT's available comparing zirconia and titanium dental implants, so this was one of the major weaknesses of this review as well designed RCT's minimise the risk of bias thus enhancing the validity of the results. Therefore, this review adopted a systematic approach rather being a true systematic review.

Another consideration is that this review could have included a meta-analysis. This could have summarised the results of the RCT's using a statistical model, which would have provided more precise results for the survival rate, success rates and MBL.

QUALITY OF STUDIES

In this review four RCT's[45,47,57,58] were included with three RCT's directly comparing titanium and zirconia implants and one comparing immediate occlusal loading to non-occlusal loading in zirconia dental implants. The quality of the RCT's was low due to high-risk bias involved therefore reducing the validity of the results in this review. The risk of bias was assessed by using the Cochrane risk-of-bias tool for randomized trials (RoB 2).[62]

Table 5. Survival and Success Rate of the included studies

Study Number	Reference	Material	Number of implants	Follow-up (months)	Survival Rate (%)	Success Rate (%)	Success Criteria
1	Lorenz *et al.* 2019	YTZP	83	93.6	100	-	-
2	Bormann *et al.*. 2018	YTZP	31	36	97.7	97.5	Buser *et al.*1990
3	Rodriguez *et al.* 2018	YTZP	24	25	92	92	NR
4	Balmer *et al.* 2017	YTZP	66	36	98.5	-	-
5	Becker *et al.* 2017	YTZP	48	24	95.8	-	-
6	Kniha *et al.* 2017	YTZP	82	12	100	100	Jahn *et al.* 1992
7	Kohal *et al.* 2017	YTZP	66	36	90.80	-	-
8	Grassi *et al.* 2015	YTZP	32	61.2	96.8 (type 1) 100 (type 4)	93.75 (type 1) 100 (type 4)	Alberktsson *et al.* 1986, Misch *et al.* 2008
9	Payer *et al.* 2015	Ti YTZP	15 16	24 24	100 93.3	100 93.3	Naert *et al.*1992 and Snauwaert *et al.* 2000
10	Roehling *et al.* 2015	YTZP	161	71.3	77.3	77.6	Buser *et al.*1990
11	Siddiqi *et al.* 2015	Ti YTZP	48 62	12 12	88.3 76.5	66.7 67.6	Alberktsson *et al.* 1998
12	Brull *et al.* 2014	YTZP	121	18.4	96.5	-	-
13	Osman *et al.* 2014	Ti YTZP	56 73	12 12	82.2 71.2	- -	-
14	Borgonovo *et al.* 2013	YTZP	28	48	100	100	-Mobility is not present -Self reported pain or paraesthesia is not present -Peri-implant radiolucency is not present -Peri-implant bone loss inferior to 1.5mm during the first year in function and an annual bone loss thereafter are not exceeding 0.2mm
15	Kohal *et al.* 2013	YTZP	56	12	98.2	-	-
16	Payer *et al.* 2013	YTZP	20	24	95	95	Naert *et al.*1992 and Snauwaert *et al.* 2000
17	Cannizzaro *et al.* 2010	YTZP	40	12	85 (immediate) 90 (conventional)	-	-
18	Olivia *et al.* 2010	YTZP	831	40.8	94.95	94.65	-No mobility -No pain -No peri-implant mucositis -No peri-implant bone loss -No implant fracture

Key: Ti= titanium, YTZP= yttria-stabilised tetragonal zirconia polycrystal, NR= not recorded , -= not investigated

The randomization process of allocating patients in two the of the RCT's[45,47] was computer generated and in one RCT[58] it was performed manually with sealed envelopes which reduced the risk of bias and distributed the confounding factors evenly. The fourth RCT[57] did not mention an allocation process which raises some concern for bias.

In all of the RCT's, the investigators who carried out the implant surgery were aware of intervention the patient received. This is a major limitation in surgical procedures as it is difficult to double blind patients and investigators. Therefore, there would have been some risk of bias from the investigators even if it was unintentional.

Table 6. MBL of the included studies

Study Number	Reference	Material	Number of implants	Mean MBL (mm)	Radiograph	Reference Point	Sites Measured	Investigators
1	Lorenz *et al.* 2019	YTZP	83	1.2(+-0.76)	OPG	Implant shoulder	2 (mesial, distal)	NR
2	Bormann *et al.* 2018	YTZP	31	0.97(+-0.88)	PA	Implant shoulder	2 (mesial, distal)	one independent
3	Rodriguez *et al.* 2018	YTZP	24	0.3	PA	NR	2 (mesial, distal)	two independent
4	Balmer *et al.* 2017	YTZP	66	0.7(+-0.72)	PA	NR	NR	NR
7	Kohal *et al.* 2017	YTZP	66	1.45(+-1.96)	PA	Implant abutment	NR	one independent
8	Grassi *et al.* 2015	YTZP	32 (Type 1) (Type 4)	1.29(+-0.25) 1.17 (+-0.33)	PA	Implant abutment	2 (mesial, distal)	NR
9	Payer *et al.* 2015	Ti YTZP	15 16	1.43 (+- 0.67) 1.48 (+-1.05)	PA	Implant shoulder	2 (mesial, distal)	one independent
10	Roehling *et al.* 2015	YTZP	161	0.97(+-0.07)	OPG	Implant shoulder	2 (mesial, distal)	NR
12	Brull *et al.* 2014	YTZP	121	0.13(+-0.6)	PA	NR	2 (mesial, distal)	NR
13	Osman *et al.* 2014	YTZP Ti	73 56	0.42(+-0.4) 0.18(+-0.47)	PA	Top of ball abutment	2 (mesial, distal)	two independent
14	Borgonovo *et al.* 2013	YTZP	28	1.63	PA	Implant shoulder	2 (mesial, distal)	NR
15	Kohal *et al.* 2013	YTZP	56	1.95 (+- 1.71)	PA	Implant abutment	2 (mesial, distal)	one independent
16	Payer *et al.* 2013	YTZP	20	1.29	PA	Implant shoulder	2 (mesial, distal)	one independent
17	Cannizzaro *et al.* 2010	YTZP	40 (immediate) (conventional)	0.9 (+-0.48) 0.72(+-0.48)	PA	Implant collar	2 (mesial, distal)	one non-independent

Key: PA= periapical, OPG= orthopantomogram, NR= not recorded

In one RCT[45] four different surgeons were assessed with three being first time users of zirconia dental implants and in another RCT[47] two different surgeons placed the implants. This can reduce the reliability of the studies as less experienced surgeons may have lower survival and success rates and techniques may differ even though each surgeon followed the manufactures' protocols.

All four RCT's had relatively small sample sizes, 22 (Payer *et al.*[47]), 24 (Osman *et al.*[57], Siddique *et al.*[58]) and 40 patients (Cannizzaro *et al.*[45]). In these studies, all of the data were accounted for with the number of dropouts and reasons. There were no dropouts in two of the RCT's.[45,47] In the other two RCT's 5 out of 24 participants dropped out in each of studies due to death and personal reasons.[57,58] This shows a high dropout rate as only 79% of the participants were available at follow-up which leads to risk of bias in the data collected and reduce the validity of the results.

The risk of bias for outcome measures in one of the RCT[45] was high, as one of the dentists who performed 10 of implant placements also performed the radiographic evaluations of the participants in the study. In two of the RCT's[57,58] there was some concern of bias regarding the outcome measure as it did not mention who performed the radiographic evaluation for the MBL. However, it tried to ensure inter-observer reliability by using a second investigator. There was a low risk of bias in one RCT[47] as an independent investigator was used for radiographic evaluation of MBL and in cases of questionable measurements, an additional two independent investigators were used and there was a consensus which ensured inter-observer reliability.

One RCT[45] was partially supported by Z-systems and one RCT[47] was funded by Ziterion, both being the manufacturers of the implants used in these studies, which could raise some concern in the risk of bias in selection of the reported results as they would hope to demonstrate that their implants were successful.

All of the RCT's in this review had high or some risk of bias in one of the domains, as mentioned above, which downgrades their overall quality from a level 2 (well-designed RCT with a minimal risk of bias) to level 3 (RCT which can improve study design to minimise risk of bias) according to the OCEBM Levels of Evidence.

One of the limitation of designing an RCT for a surgical intervention is that the surgeon is always going be aware of the treatment received by the patient thus introducing a risk of bias. An ethical concern in a surgical RCT is the random allocation of patients to a group. This raises concern over obtaining valid consent as the patient is not aware of the treatment they will receive. These limitations of RCT must be taken in consideration when designing future studies for surgical interventions and possible well-designed cohort studies may be a better option from ethical point of view.

In this review there were seven prospective cohort studies. These were all grade level 3 according to the OCEBM Levels of Evidence. Furthermore, this review included four prospective case series studies[46,54-56] and three retrospective case series studies[44,52,59] which was graded level 4 OCEBM Levels of Evidence.

Overall this review included 11 studies (61%) of level 3 and 7 studies (39%) of level 4 according to the OCEBM Levels of Evidence hierarchy. In scientific terms, this shows relatively poor level of evidence-based practice.

STRENGTH AND WEAKNESS OF INCLUDED STUDIES

Patient demographics

The first weakness of some of the included studies was the small sample size. The number of zirconia implants placed in the studies ranged from 16 (Payer *et al.*[47]) to 831 (Oliva *et al.*[55]). The small sample can reduce the statistical power of the study therefore making the results less reliable.

Eleven of the eighteen studies recruited their population solely from prosthetic and maxillofacial departments at university hospitals.[43,44,46,47,49,51,54,56-58,60] This can make the investigations more biased as patients referred to secondary care generally have more complex needs beyond the scope of the general dental practitioner. Therefore, the generalisability of the results to the general population is poor.

Surprisingly, many of the studies included in this review included patients who smoked. A systematic review showed smoking significantly affects the failure rates and MBL of implants.[63] This could have been a confounding factor for high MBL seen in two studies[46,49] which did not mention the exclusion of smokers from their population sample. A further study[59] also included smokers but did not quantify how many and this could have led to the poorer survival and success rates achieved in their study. Another cofounding factor which could lead to the high MBL in the two studies could have been due to active periodontitis or patients with no regular periodontal maintenance care. Only 50% of the studies included in this review excluded patients with active periodontitis or without regular periodontal maintenance care. Finally, not all of the included studies excluded patients that had bruxism as mentioned earlier bruxism causes occlusal overload which leads to MBL. This emphasises the need for stricter exclusion criteria in the future studies so that the confounding factors are reduced thus increasing the reliability of the results. From an ethical point of view, it raises the question should the patients have received the implants in the first instance, if they were smokers or had active periodontitis.

In the included studies another limitation was that patients were not followed up for a long period of time, only 3 studies had follow-up more than 60 months (5years).[43,48,59] The maximum follow-up period in the included studies was 93.6 months,[43] just under 8 years. This can make it difficult to assess the long-term survival and success rate of zirconia dental implants. This can also have an ethical implication in regard to explaining to the patient the long-term prognosis of zirconia implants in the process of obtaining valid consent when the long-term prognosis is unknown.

Implant characteristics

Roehling *et al.*[59] study showed a low survival rate and success rate, 77.3% and 77.6% at 71.3 months. This could have been due the narrow diameter (3.25) implants which displayed a survival rate of 58.5%. A systematic review showed that narrower implants (<3.3 mm) had lower survival rates compared with wider implants (≥3.3 mm).[64] This is reflected by the results of Roehling *et al.*[59] study.

Surgical characteristics

One RCT included in this review showed a small difference in survival rate in immediately loaded compared with conventionally loaded implants, 85% to 90% at 12 months.[45] It showed slightly less MBL for conventionally loaded to immediately loaded 0.72 +-0.48mm to 0.9+-0.48mm at 12 months. This study also reported that zirconia implants placed in immediate post-extraction sites showed higher risk of failure than implants placed at healed sites. This result has to be interpreted with caution due to the high risk of bias caused by small sample size, different surgeon experience and the investigator measuring MBL who also performed some of the implant placements.

Survival and Success rate

There was generally homogeneity in defining the survival of implants in all the studies, the implant was present in the mouth at the recall appointment independent of biological and/or technical complications. This homogeneity makes it easier to compare the results of each of the studies but in clinical terms does not provide sufficient information on how the implant performed.

There was heterogeneity in defining the success of an implant in the studies. Table 5 demonstrates that many success criteria were used throughout the studies. This can lead to variability in the success rate of a zirconia implant and make it difficult to compare results of one study to another. Many

of the factors in the criteria were subjective such as pain and mobility which affect the reliability of the success rate recorded in the studies.

The Osman *et al*.[57] and Siddiqi *et al*.[58] studies showed the lowest survival rate and success rate from the 18 studies included in this review. This could have been because they were the only two studies in which implants were placed mid-palatal in the maxilla to aid the retention of overdenture prostheses. The Siddiqi *et al*.[58] study found a 50% survival rate of mid-palatal implants and Osman *et al*.[57] study achieved a 55% survival rate for mid palatal zirconia implants which could have led them to poorer survival rates than in the other studies.

Marginal bone loss

The methodology for measuring the MBL varied from study to study, therefore making it difficult to compare each of the studies directly. All of the studies carried out radiographic measurements using computer software. This was good as it reduced human measurement errors thus increasing the precision of the results. However, some studies did not mention the reference points thus making the repeatability of this studies difficult and questions their accuracy in measuring the MBL.

Most of the studies measured the MBL at mesial and distal surfaces on the radiographs and calibrated their measurements using a known length, diameter or thread spacing which ensured their results were more accurate and reliable. An implant has many other surfaces such as buccal or lingual, therefore this raises an issue in that is the MBL measured in the studies representative of actual MBL that has occurred when the other surfaces have not been accounted for.

All of the studies used radiographs either periapical or OPG at subsequent recall intervals to evaluate the MBL. This raises concern's in terms of the accuracy of reproducing the same radiograph at the same angle and position as the initial one. This discrepancy can lead to over or under measuring MBL than the actual MBL occurred which affect the reliability of the results.

According to the ICOI 2007 criteria, mentioned earlier in this review, an MBL of less than 2mm around the implant neck during the first year of function is deemed successful. All fourteen studies that recorded the mean MBL would meet this criterion but when considering the standard deviation three studies exceeded the 2mm in their follow-up period and did not meet the criterion.[46,47,49]

As the ICOI 2007 criteria mentions the first year in function and two of the studies were followed up for a longer period, a further analysis revealed the mean MBL after 12 months in Payer *et al*.[47] RCT was 1.16+-1.01mm for zirconia implants and 0.88 +- 0.56mm for titanium implants and in the Kohal *et al*.[49] study it was 1.3+-1.49mm for the zirconia implants. This shows the criterion was met for titanium implants but was not met for zirconia implants in the RCT. Interestingly both the Kohal *et al*.[4649] studies did not record the success rates for zirconia implants and only recorded the survival rates. This could have been attributed to the significant MBL of their zirconia implants. Furthermore, in the Payer *et al*.[47] study there was no mention of bone loss in their success criteria which could have attributed to their high success rate of 93.3%.

Comparing results to previous studies

A study solely investigating titanium implants showed a 98% survival rate and 95.9% success rate with a mean marginal bone loss of 0.76 ± 0.47 mm at 6 years.[65] Another study reported a survival rate of 98.8% and a success rate of 97% at 10 years for titanium implants.[66] These studies demonstrate a high survival and success rates for titanium dental implants.

A previous review[22] performed a meta-analysis of the three RCT's[47,57,58] included in this review and found the survival rate at 12-24 months of zirconia implant was 74.8%, which was lower than for titanium implants at 85%. They also found the success rate of the zirconia implants was not very different to titanium implants. They found the mean MBL difference of 0.14mm between titanium and zirconia implants which showed similar MBL for each implant material. These results are similar to the results obtained in this review.

Another review showed that zirconia could be an alternative to titanium implants, but more long-term studies are needed.[67] The need for long-term studies was also reflected in this review as the long-term survival and success rates of zirconia implants is not known.

CONCLUSIONS

After reviewing the literature on the survival rate, success rate and MBL for zirconia implants the following conclusions can be made:

Primary aim

1. The three RCT's included in this review directly comparing zirconia implants to titanium implants, the survival rate was lower for zirconia implants, but the success rate was found to be similar.
2. The studies solely investigating zirconia implants generally showed high survival and success rates. The survival rate and success rate achieved was 90% and above 92% except in one study.

Secondary aim

1. The RCT's included in this review showed similar MBL between zirconia and titanium implants.
2. The studies solely investigating zirconia implants generally showed less than 2mm except in two of the studies.

RECOMMENDATIONS

To provide a better level of evidence for clinicians on the use of zirconia implants the following recommendations can be made:

- More well-designed studies comparing zirconia and titanium implants with a larger and representative population sample and longer follow-up period need to be performed.
- The need for uniformity in methodologies in defining success of dental implant and measuring the MBL so that results of different studies can be compared to each other.

SUMMARY

Overall zirconia dental implants are showing promise as an alternative to titanium implants to be used in general practice. However, there is a need for further well-designed studies to be carried out to assess their long-term survival rate, success rate and MBL. At present, zirconia implants should be used with caution but can be an alternative option if patient has an absolute contraindication to titanium due to a titanium allergy.

CONFLICT OF INTEREST AND SOURCE OF FUNDING STATEMENT

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