Comparison of Clinical Performance of Zirconia Implants and Titanium Implants in Animal Models: A Systematic Review

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Purpose: *This study aimed to compare the values of removal torque (RT) and bone-implant contact (BIC) reported in different animal studies for zirconia and titanium implants.* ***Materials and Methods:*** *A systematic review of the literature was performed to analyze BIC and RT of animal studies in which both zirconia and titanium dental implants were used. To identify the studies to include in this systematic review, an exhaustive search of PubMed was performed of animal studies published in English with reports on the quantification of the osseointegration of both titanium and zirconia implants by means of BIC and/or RT. The results were aggregated and analyzed within each of the animal models (pig, rabbit, rat, monkey, dog, and sheep).* ***Results:*** *The selection process resulted in a final sample of 16 studies. In general, no significant differences were found between titanium and zirconia. The significant differences in terms of BIC and RT reported by the authors were attributable to the different surface treatments and microporosities of the implant surfaces studied, not to the materials themselves. Only two articles reported significantly lower BIC for modified zirconia implants as compared to modified titanium implants. Four authors described statistically significant differences in terms of RT between zirconia and titanium implants in the different animal models, regardless of the surface treatment received by the implants.* ***Conclusions:*** *Within the limitations of this study, the values for the BIC and RT of zirconia implants in most of the studies analyzed did not show statistical differences compared with titanium implants. Modified-surface zirconia may have potential as a candidate for a successful implant material, although further clinical studies are necessary.* Int J Oral Maxillofac Implants 2014;29:311–320. doi: 10.11607/jomi.2817

Key words: *dental implants, titanium, zirconia*

The replacement of teeth with dental implants in partially or completely edentulous patients is a widely accepted and documented treatment modality.[1–5] The materials most commonly used for this purpose are commercially pure titanium and titanium alloys because of their biocompatibility and excellent mechanical properties.[1–3] Commercially pure titanium has different degrees of purity (grades 1 to 4), as characterized by oxygen, iron, and carbon content.[6] Most implants are made of grade 4 titanium, since it is stronger than the other grades.[6] Titanium alloys are typically titanium-aluminum-vanadium (Ti-6Al-4V) (grade 5 titanium alloy), which has greater strength and fatigue resistance than pure titanium.[6]

Since the introduction by Brånemark et al[1,2] of the biologic concept of osseointegration, defined as a direct structural and functional connection between ordered living bone and the surface of a load-carrying implant, titanium has been considered the gold standard material used for dental implants.[1–5] Ten-year survival rates above 95% and 15-year survival rates above 90% have been reported[3,5,7] for machined titanium implants.

Zirconia has been proposed as an alternative to titanium as an implant material primarily for esthetic reasons.[8] When titanium implants are used, especially in anterior sites in the mouth, they can produce poor esthetics; the greyish color of the implant body is exposed after soft tissue recession or if a thin gingival biotype is present. The material of zirconia implants is yttria-stabilized zirconia ceramic (Y-TZP), which

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Table 1 Excluded Articles and Reasons for Exclusion

Study	Reason for exclusion
Ozkurt et al[20]	Not an animal study
Caneva et al[21]	Focused on collagen membranes
Andreiotelly et al[8]	Review article
Tetè et al[14]	Focused on soft tissues around the implants
Alzubaydi et al[22]	Compared zirconia and titanium abutments, but not implants
Wenz et al[9]	Review article
Franchi et al[23]	Studied different surface treatments of titanium implants; did not compare titanium to zirconia
Kong et al[24]	Did not compare titanium to zirconia
Dubruille et al[25]	Parameters studied were not BIC and RTQ

has flexural strength between 900 and 1,200 MPa, a Young's modulus of 200 to 210 GPa, and a fracture resistance of 7 to 10 MPa.[9]

The use of zirconia in orthopedic surgery has been controversial, because at low temperatures (but above room temperature) and in humid environments, zirconia undergoes a phase transition (from tetragonal to monoclinic), leading to material degradation and possibly great reductions in mechanical strength.[10] This hydroscopic degradation was why in 2001 about 400 femoral heads failed in a very short time.[11] To solve this problem, the zirconia was stabilized with yttria.[10]

In dentistry, Y-TZP has been used for all-ceramic fixed partial restorations as well as for all-ceramic implant abutments.[12] Many studies have shown that the biocompatibility of zirconia is equal to that of titanium, with no negative effects on hard or soft tissues, and the accumulation of plaque is lower than in titanium implants.[13,14] Because high concentrations of radioactive elements are present in the raw material used to manufacture zirconia powder, the possibility of exposure to radiation via zirconia implants has been discussed.[15] This radioactivity is a result of the impurities present in zirconia that render a Y-TZP purification process essential.[11] Because the conventional manufacture of zirconia implants results in a rather smooth surface, and since several studies have shown that modifications of roughness and topography can improve the osseointegration of these implants,[16,17] many authors have analyzed modifications of the surface of zirconia implants.

Two methods are commonly used to assess the quality of osseointegration in a quantitative manner: bone-to-implant contact (BIC) and removal torque (RTQ). RTQ is a quantitative mechanical method for assessing osseointegration that calculates the torsional strengths needed to remove an inserted implant.[18] BIC is a histomorphometric measure that estimates the percentage of mature bone in direct contact with the implant surface in microscopic specimens, providing a biologic estimation of the behavior of the bone around the implant surface.[19]

Clinicians should know the differences, if any, in performance of zirconia versus titanium implants in terms of the quality of osseointegration as quantified with BIC and RTQ. The aim of the present work was to collect and compare the clinical results from animal studies in which the osseointegration of both titanium and zirconia implants was measured with RTQ, BIC, or both.

MATERIALS AND METHODS

To identify studies eligible for inclusion in this systematic review, in May 2013 an exhaustive search strategy was performed in the PubMed database using the following search strategy: ((("Zirconium"[Mesh] AND "Titanium"[Mesh]) AND "Dental Implants"[Majr]) AND "Osseointegration"[Mesh] NOT "Abutments"). The search was limited to animal studies published in English with reports on the quantification of the osseointegration of both titanium and zirconia implants by means of BIC and/or RTQ. After the abstracts were reviewed, all the papers fulfilling the selection criteria were included and the full texts of all articles were obtained. The reference list of included articles was revised manually to incorporate additional eligible publications.

RESULTS

Initially, 28 papers in which this strategy was used were retrieved, but only 19 fulfilled the inclusion criteria. Table 1 lists the nine articles that were excluded.[8,9,14,20–25] The included studies addressed the behavior of titanium and zirconia implants in six animal models: minipigs,[17,26–35] rabbits,[35–39] rats,[40] monkeys,[13] sheep,[16,17] and dogs.[41] In one study[13] the implants were loaded functionally, while in the remaining 18 articles the implants were not loaded.

Brief descriptions of the main results of each included study are given in Table 2 (BIC) and Table 3 (RTQ). Figure 1 summarizes the aggregated BIC and RTQ data obtained from the reviewed studies performed on the most common animal models (pigs and rabbits). A similar quality of osseointegration throughout the follow-up period was observed in both animal models, even when the surface treatment was not always equivalent for zirconia and titanium.

Table 2 BIC Reported in the Analyzed Studies

Author/year	Animal (no. and type)	Location	Follow-up	Implants (no. and material)	Mean BIC (%)
Kohal et al[13] (2004)	6 monkeys	Maxilla	6 mo	12 Ti-S-E	73
				12 Zi-S	67
Sennerby et al[36] (2005)	12 rabbits	Femur	6 wk	24 Ti	68
		Tibia			47
		Femur		24 Zi A	60
		Tibia			56
		Femur		24 Zi B	70
		Tibia			47
		Femur		24 Zi M	46
		Tibia			36
Depprich et al[42] (2008)	12 minipigs	Tibia	1 wk	24 Ti E	48
			4 wk		59
			12 wk		83
			1 wk	24 Zi E	35
			4 wk		45
			12 wk		71
Hoffmann et al[37] (2008)	4 rabbits	Femur	2 wk	4 Ti	48
			4 wk		80
			2 wk	4 Zi S	55
			4 wk		72
Lee et al[38] (2009)	40 rabbits	Femur	3 wk	20 Ti	78
			6 wk		67
			3 wk	20 Zi	71
			6 wk		70
			3 wk	20 Zi CaP I	65* (Ti)
			6 wk		69
			3 wk	20 Zi CaP SP	62* (Ti)
			6 wk		65
Kohal et al[12] (2009)	42 rats	Femur	14 d	21 Ti M	23
			28 d		39
			14 d	21 Ti Unite	36
			28 d		55
			14 d	21 Zi M	31
			28 d		47
			14 d	21 Zi MO	45
			28 d		59
Gahlert et al[28] (2009)	15 pigs	Maxilla	4 wk	15 Ti	24
			8 wk		53
			12 wk		59
			4 wk	15 Zi	27
			8 wk		52
			12 wk		52
Rocchietta et al[39] (2009)	18 rabbits	Femur	3 wk	20 Ti Unite	32
		Tibia			64
		Femur		41 Zi Unite	43
		Tibia			43
		Femur		41 Zi H I	43
		Tibia			43
		Femur		41 Zi H SP	48
		Tibia			36

Table 2 *continued* BIC Reported in the Analyzed Studies

Author/year	Animal (no. and type)	Location	Follow-up	Implants (no. and material)	Mean BIC (%)
Stadlinger et al[29] (2010)	7 minipigs	Maxilla	4 mo	7 Ti S-E Sub	53
				7 Zi S Sub	53
				7 Zi S N-Sub	48
Schliephake et al[30] (2010)	12 minipigs	Maxilla	4 wk	24 Ti S-E	69
			13 wk		79
			4 wk	24 Zi S	58
			13 wk		55* (Ti S-E)
			4 wk	24 Zi S-E	67
			13 wk		58* (Ti S-E)
Koch et al[41] (2010)	6 dogs	Mandible	4 mo	12 Ti S	41
				12 Zi S	59
				12 Zi S Ca coat	56
				12 PEEK	26
Shin et al[35] (2011)	5 rabbits	Tibia	6 wk	Ti M	36
				Zi M	26
Hoffmann et al[34] (2012)	48 rabbits	Femur	6 wk	Ti	34
				Zi laser	40
				Zi S	40
				Zi sint	33
			12 wk	Ti	35
				Zi laser	44
				Zi S	41
				Zi sint	34
Möller et al[31] (2012)	8 pigs	Frontal	4 wk	Ti	69
				Zi	59
			12 wk	Ti	74
				Zi	67
Gahlert et al[33] (2012)	18 minipigs	Maxilla	4 wk	Ti	65
				Zi	70
			8 wk	Ti	79
				Zi	67
			12 wk	Ti	84
				Zi	68

Ti = titanium; Zi = zirconia; Ca = calcium; S = sandblasted; Sub = submerged; E = etched; M = machined; I = immersion; N-Sub = nonsubmerged; SP = sprayed; MO = modified; H = hydroxyapatite; E = etched; sint = sintered; PEEK = polyetheretherketone.
*Significantly lower values than the subgroup used in brackets ($P < .05$).

BIC Analysis

Regarding titanium implants (Table 2), in rabbits, BIC as a measure of osseointegration ranged from 32%, evaluated in the femur after 3 weeks,[39] to 80%, evaluated in the femur after 4 weeks.[37] In minipigs, this value ranged from 24% after 4 weeks in the maxilla[28] to 83% after 12 weeks in the tibia.[44]

With respect to zirconia implants (Table 2), in rabbits the BIC ratio as a measure of osseointegration ranged from 36%, evaluated in the tibia after 6 weeks,[36] to 72%, evaluated in the femur after 4 weeks.[37] In minipigs it ranged from 27% in the maxilla after 4 weeks[28] to 71% after 12 weeks in the tibia.[42] In sum, most of the reviewed articles did not report significant differences in BIC between groups.[13,15,17,27–29,31,33–37,39,41] Only two articles[30,38] reported significantly lower values for zirconia as compared to titanium implants (Table 2). In the study performed by Schliephake et al,[30] the BIC and RTQ of three different types of implants placed in the maxilla of 12 minipigs were compared. The implants were sandblasted and etched titanium, zirconia sandblasted with corundum (aluminum oxide), and sandblasted and etched zirconia. At 4 weeks, no significant differences were found in BIC among the three groups, but BIC was significantly lower for zirconia implants after 13 weeks of healing because of an increase in the BIC in the titanium implants. Lee et al[38] evaluated the BIC of titanium implants and zirconia implants. The groups were as follows: untreated titanium implants, untreated zirconia implants, zirconia implants coated

Table 3 RTQ Values Reported in the Analyzed Studies

Author/year	Animal (no. and type)	Location	Follow-up	Implants (no. and material)	Mean RTQ (Ncm)
Sennerby et al[36] (2005)	12 rabbits	Femur	6 wk	24 Ti	74
		Tibia			42
		Femur		24 Zi A	98
		Tibia			47
		Femur		24 Zi B	85
		Tibia			58
		Femur		24 Zi M	20*
		Tibia			12*
Gahlert et al[26] (2007)	13 minipigs	Maxilla	12 wk	18 Ti	105
				23 Zi M	26* (Ti and Zi S)
				23 Zi S	41* (Ti)
Ferguson et al[16] (2008)	15 sheep	Iliac crest	2 wk	Ti	73
			4 wk		141
			8 wk		188
			2 wk	Ti+CaP	66
			4 wk		130
			8 wk		168
			2 wk	Ti+CaP anod	59
			4 wk		78
			8 wk		92* (Ti and Ti+CaP and Ti+alendronate and Ti+collagen)
			2 wk	Ti+alendronate	87
			4 wk		144
			8 wk		184
			2 wk	Ti+collagen	68
			4 wk		146
			8 wk		159
			2 wk	Zi	55
			4 wk		87
			8 wk		100* (Ti and Ti+CaP and Ti+alendronate and Ti+collagen)
Kohal et al[12] (2009)	42 rats	Femur	28 d	21 Ti M	7
				21 Ti Unite	34
				21 Zi M	9
				21 Zi MO	46
Rocchietta et al[39] (2009)	18 rabbits	Femur	3 wk	41 Zi Unite	32
		Tibia			26
		Femur		41 Zi H I	33
		Tibia			41
		Femur		41 Zi H SP	41
		Tibia			27
Schliephake et al[30] (2010)	12 minipigs	Maxilla	4 wk	24 Ti S-E	245
				24 Zi S	56* (Ti S-E and Zi S-E)
				24 Zi S-E	112** (Ti S-E)
			13 wk	24 Ti S-E	222
				24 Zi S	99* (Ti S-E and Zi S-E)
				24 Zi S-E	100**(Ti S-E)
				Zi laser	26
				Zi S	20* (Ti and Zi sint)
				Zi Sint.	35
			12 wk	Ti	52
				Zi laser	40
				Zi S	29* (Ti)
				Zi sint	41

Table 3 *continued* RTQ Values Reported in the Analyzed Studies

Author/year	Animal (no. and type)	Location	Follow-up	Implants (no. and material)	Mean RTQ (Ncm)
Gahlert et al[32] (2010)	16 minipigs	Maxilla	4 wk	Ti S-E	42
				Zi S-E	42
			8 wk	Ti S-E	75
				Zi S-E	70
			12 wk	Ti S-E	73
				Zi S-E	70
Shin et al[35] (2011)	5 rabbits	Tibia	6 wk	Ti M	11
				Zi M	18
Hoffmann et al[34] (2012)	48 rabbits	Femur	6 wk	Ti	40
				Zi laser	26
				Zi S	20* (Ti and Zi sint)
				Zi sint	35
			12 wk	Ti	52
				Zi laser	40
				Zi S	29* (Ti)
				Zi sint	41

Ti = titanium; Zi = zirconia; S = sandblasted; Sub = submerged; E = etched; M = machined; I = immersion; N-Sub = nonsubmerged; sint = sintered; SP = sprayed; MO = modified; H = hydroxyapatite.
*Significantly lower values than the subgroup used in brackets ($P < .05$). **Significantly lower values than the subgroup used in brackets ($P < .01$).

with calcium phosphate (CaP) by immersion, and zirconia implants coated with CaP by spraying. The study was carried out in 40 rabbits, which were monitored for 3 weeks (n = 20) or 6 weeks (n = 20). The BIC at 3 weeks was significantly greater for the titanium implants, but at 6 weeks there were no significant differences. In conclusion, these authors found that all the surfaces studied were osteoconductive, but that this property was not improved by CaP coating of the zirconia implants.

RTQ Analysis

Regarding titanium implants (Table 3), in rabbits, RTQ as a measure of osseointegration ranged from 42 Ncm in the tibia after 6 weeks[36] to 74 Ncm in the femur after 6 weeks.[36] In minipigs, in the maxilla, paradoxically, the values decreased, from 245 Ncm after 4 weeks[30] to 105 Ncm after 12 weeks.[26]

In the case of zirconia implants (Table 3), in rabbits, RTQ ranged from 12 Ncm in the tibia after 6 weeks[36] to 98 Ncm in the femur after 6 weeks.[36] In minipigs, in the maxilla, these values, as observed for titanium implants, decreased from 112 Ncm after 4 weeks[30] to 26 Ncm after 12 weeks.[26] Four of the articles reviewed reported no significant differences in RTQ between different groups of zirconia and titanium implants.[12,32,35,39] Five studies[16,26,30,34,36] reported significantly lower RTQ for zirconia implants than for titanium implants (Table 3).

For example, Ferguson et al[16] and Langhoff et al[17] studied both BIC and RTQ in 15 sheep sacrificed at 2, 4, and 8 weeks. The implant subgroups were: (*1*) titanium modified by sandblasting and acid etching; *(2)* zirconia modified by sandblasting and acid etching; *(3)* titanium sandblasted, etched, and coated with CaP by immersion in an aqueous solution of CaP; *(4)* titanium sandblasted, etched, and coated with CaP by anodization; *(5)* titanium sandblasted, etched, and coated with bisphosphonate (alendronate); and *(6)* titanium sandblasted, etched, and coated with type I collagen and chondroitin sulfate. With respect to RTQ, at 2 and 4 weeks there were no statistically significant differences between the six subgroups. After 8 weeks, the RTQ values of groups 1, 3, 5, and 6 were statistically higher than in groups 2 and 4.[16] By contrast, regarding BIC at weeks 2, 4, and 8, no significant differences were found between any of the implants, and hence, it was concluded that neither chemical nor pharmacologic modifications improved osseointegration.[16,17]

In another animal study, Gahlert et al[26] placed three different types of implants in minipigs: 18 titanium implants, 23 machined zirconia implants, and 23 zirconia implants modified by sandblasting the surface with corundum. RTQ was assessed at 4, 8, and 12 weeks. At each of these time points, the RTQ values were significantly greater for titanium than for zirconia implants, but they were also higher for the modified zirconia implants than for the machined zirconia implants. These findings suggest that the modified zirconia implants achieved greater stability in bone than machined zirconia implants.[26]

Schliephake et al[30] compared the BIC and RTQ of three different types of implants placed in the maxillae of 12 minipigs. The BIC results were discussed earlier.

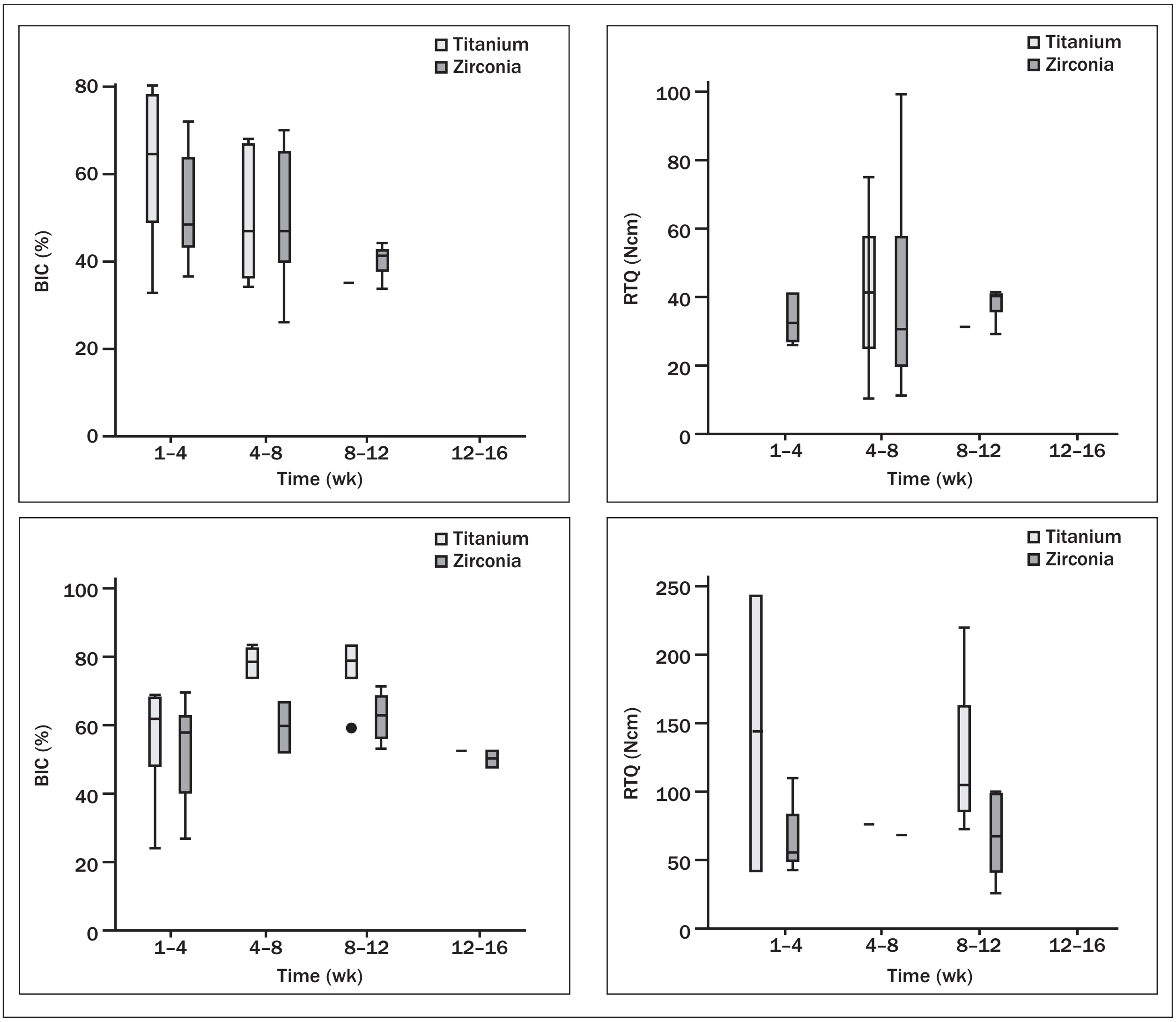

Fig 1 Box plots of BIC and RTQ using aggregated data from the reviewed studies on *(top)* rabbits and *(bottom)* pigs.

Regarding the RTQ results, at 4 weeks the RTQ was significantly higher for sandblasted and etched zirconia implants than for sandblasted zirconia implants. The RTQ values were also significantly higher for the titanium implants as compared with both types of zirconia implants. However, at 13 weeks there were no differences between the two zirconia implants, while the titanium implants showed a significantly higher RTQ than the zirconia implants.

Hoffmann et al[34] evaluated four types of implants (sintered zirconia, laser-modified zirconia, sandblasted zirconia, and acid-etched titanium) in rabbits. The specimens were harvested at 6 or 12 weeks and evaluated for RTQ. The differences in RTQ were significantly different between titanium and sandblasted zirconia and between sintered zirconia and sandblasted zirconia, with the former demonstrating higher RTQ at 6 weeks. At 12 weeks, the titanium implants demonstrated a significantly higher RTQ than the sandblasted zirconia implants. However, Hoffmann et al concluded that RTQ was similar for all types of implants with a roughened surface.

Finally, in a rabbit-based study, Sennerby et al[36] investigated the bone tissue response (by means of BIC and RTQ) around four types of implants histologically and biomechanically: zirconia implants with A porosity, zirconia implants with B porosity, machined zirconia implants, and oxidized titanium implants. After 6 weeks of follow-up, no significant differences were found between the different implants in terms of BIC. However, the RTQ values were significantly higher for the titanium (42 to 72 Ncm) and modified zirconia A (47 to 98 Ncm) or B (58 to 85 Ncm) implants with respect to the machined zirconia implants (12 to 20 Ncm).

DISCUSSION

This systematic review focuses on measuring the likely clinical performance of both titanium and zirconia implants by estimating the quality of osseointegration through BIC and/or RTQ in animal studies. The methodology applied for this revision followed the recommendations of the QUOROM guidelines recommended by the International Committee of Medical Journal Editors (www.icmje.org). However, it should be acknowledged that the exclusive use of the PubMed database to search for papers may not have captured all the available literature, although it certainly captured the majority and the most relevant studies.

Most of the included studies observed a healing period for assessing zirconia and titanium implants between 14 days and 6 months. The implants were placed in different animal models (from rats to monkeys), in different locations, and under different loading conditions (mostly not loaded). Additionally, most of the studies were performed in rabbits (usually on femurs or tibias) and minipigs (in the maxilla).

In these studies, the bone reacted with zirconia implants similarly to titanium implants[28,29,36,38,41,42] or even better in the initial healing period.[12,37,39] However, other authors observed a trend toward a better BIC for titanium implants.[13,27,30] It should be kept in mind that most studies were performed in a small sample of animals ($n \leq 15$ individuals) and assessed different follow-up periods, thus considerably reducing the statistical power for the detection of significant differences.

One parameter that is known to improve the process of early bone formation is modification of the implant surface.[16,17] Several studies have shown that greater roughness of the implant surface results in higher BIC.[37–41] In the present review, three studies[12,20,30] compared machined zirconia implants and sandblasted zirconia implants in the same experimental animal and found a higher BIC[12,36] for the implants with a modified surface. However, these differences were not significant, while the RTQ[12,26,36] was significantly higher in implants with a modified surface. Implants coated with different materials have also been studied to try to improve the osseointegration of zirconia implants: CaP,[38] hydroxyapatite,[39] and Ca.[41] Nevertheless, in the studies of Lee et al[38] and Rocchietta et al,[39] these coating procedures did not provide any benefit with respect to zirconia implants modified by sandblasting. Koch et al[41] found that zirconia implants coated with Ca preserved more crestal bone, but this improvement was not significant compared to uncoated zirconia implants. Nevertheless, those authors concluded that the preservation of crestal bone could have been a result of the calcium coating.

Another factor that should be addressed in future studies is the effect of implant loading. Of the articles reviewed, only one evaluated implant loading.[13] After a loading period of 5 months, there were no significant differences in BIC between the titanium (sandblasted and etched) and zirconia implants (sandblasted), although BIC was higher in the former.[13] No differences between either type of implant were observed in the peri-implant tissue. When zirconia and titanium implants are compared directly, both should have an equivalent surface treatment, because RTQ and BIC may be affected by the difference in surface roughness and not by the material. It should be noted that the macroscopic design of the implants (screw type, conical or cylindric, etc) should also be equivalent.

In the studies reviewed, RTQ was significantly higher for zirconia implants with a modified surface than for machined zirconia implants.[12,26,36] However, when modified titanium implants were compared with modified zirconia implants, the RTQ values were similar (Table 3).

Of all the articles studied, only six[13,26,28–30,41] were carried out in the mouth. Further split-mouth studies would be necessary to analyze the degradation of zirconia implants in the mouth. In a moist environment, the strength of zirconia ceramics may be decreased because of their high susceptibility to subcritical crack growth,[48] and the yttria concentration may decrease, such that the long-term clinical serviceability of the Y-TZP ceramic might be compromised by this effect.[49] In addition, studies assessing clinical performance after functional loading to determine whether zirconia implants work as well as titanium implants are scarce. Before the results of animal studies can be applied to the clinical setting, an exhaustive clinical and histomorphometric evaluation of each individual case should be carried out after a period of occlusal loading.

Further studies should be directed toward several lines of research, such as the best surface treatment for zirconia, the influence of loading and microbiologic contamination, and soft tissue responses. A more detailed description of the type of surface modifications applied to the implants (at least with regard to porosity and granulometry) should have been included in the methodology of the published papers to improve the comparability of the studies and enhance research insights for reviewers.

CONCLUSIONS

An analysis of 19 animal studies found a similar degree of osseointegration in terms of bone-implant contact and removal torque between zirconia implants and titanium implants when similar equivalent surface treatments were compared.

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