Revue systématique sur le taux de survie des implants en zircone

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PARTIE FRANÇAISE

RÉSUMÉ

OBJECTIFS

Le but de cette revue était d'évaluer d'une part les taux de succès et de survie des implants céramiques en zircone une année après leur mise en charge et, d'autre part, de juger en fonction de l'évidence scientifique si ceux-ci peuvent être considérés comme une alternative aux implants en titane.

MATÉRIEL ET MÉTHODES

Une recherche électronique dans les bases de données MEDLINE, EMBASE et Cochrane Central Register of Controlled Clinical Trials (CENTRAL) a été conduite en avril 2015 par deux examinateurs indépendants dans le but de sélectionner des études cliniques rapportant le taux de survie des implants en zircone mis en charge pendant au moins un an. Le taux de survie global des implants a été estimé en utilisant la proportion globale décrite dans les études avec un intervalle de confiance Clopper-Pearson de 95%.

RÉSULTATS

Sur les 1519 articles identifiés initialement, 14 articles ont été retenus. Après une année de mise en charge, le taux de survie global des implants en zircone une et deux pièces a été calculé à 92% (intervalle de confiance à 95% : 87-95). Concernant les taux de survie à un an des implants, les études sélectionnées ont révélé une considérable hétérogénéité.

CONCLUSION

Malgré le manque d'évidence sur le long terme permettant de justifier leur utilisation, les implants en zircone pourraient représenter une alternative au titane afin de proposer une solution « sans –métal ». Néanmoins, d'autres études cliniques sont nécessaires afin de fournir des résultats à long-terme, et de déterminer les risques de complications techniques et biologiques. Concernant les implants en zircone deux pièces, des études randomisées et contrôlées supplémentaires sont requises afin de comparer leurs taux de survie et de succès avec ceux en titane et en zircone une pièce.

IMPACT CLINIQUE

Les implants en zircone offrent une alternative potentielle au titane. Toutefois, les cliniciens doivent être conscients du manque de résultats à long-terme et d'explications sur les causes d'échecs.

Dans un monde dominé par une demande esthétique toujours plus forte, les céramiques ont gagné en popularité dans l'industrie dentaire. De nos jours, elles sont rentrées dans la confection de restaurations « tout céramique » pour dents et implants, sous forme de facettes et de piliers, ainsi que dans la production d'implants dentaires. Les céramiques à base d'alumine (Al_2O_3) et constituées de cristaux de zircone tétragonaux stabilisés à l'oxyde d'yttrium sont actuellement les matériaux de choix pour les piliers céramiques (1). Pourtant, en implantologie, la céramique zircone a montré des propriétés mécaniques supérieures à celles des autres céramiques d'un point de vue résistance à la flexion et à la fracture (2). Dans le domaine de l'implantologie, la céramique zircone est devenue une alternative intéressante au titane grâce à son faible module d'élasticité et de conductivité thermique, sa faible affinité à l'accumulation de plaque, sa haute biocompatibilité et sa couleur blanche (3-6). Néanmoins, la dégradation à basse température, également nommée « vieillissement », est considérée comme un désavantage majeur de la zircone. Il s'agit d'un processus au cours duquel la phase quadratique se transforme progressivement et spontanément en phase monoclinique sous l'action de molécules d'eau à des températures supérieures à 200°C. Il en résulte la formation de microfissures de surface pouvant progresser en profondeur et ainsi réduire drastiquement les propriétés mécaniques de la zircone, telles que sa dureté ou sa densité. Cependant, la réduction des tailles des grains et/ou l'augmentation de la concentration des stabilisants peuvent freiner ce taux de transformation (7). La ténacité de la zircone a été testée dans une étude in vitro. Les auteurs ont observé une diminution de la résistance à la fracture si les implants en zircone étaient préparés et soumis à une contrainte cyclique. Néanmoins, ils rapportèrent que même des implants avec une faible ténacité peuvent résister à une charge occlusale moyenne exercée à des intervalles étendus (8). Malgré ces limitations, plusieurs études animales ont démontré que les implants en zircone possédaient une biocompatibilité et une ostéo-intégration comparables, voire supérieures, aux implants en titane (4, 9-14). Une revue systématique (12) évaluant l'ostéo-intégration et le taux de succès des implants en zircone dans les études animales a décrit un contact os-implant supérieur à 60%. L'une d'entre elles a également rapporté une meilleure guérison osseuse autour de cônes en zircone que ceux en titane (15). Indépendamment de ces bons résultats, les auteurs ne pouvaient pas recommander l'utilisation des implants dentaires en zircone du fait d'un manque de recul sur le long terme. Une autre revue systématique (2) a inclus des études animales et humaines sur les implants en alumine et en zircone. Les auteurs ont conclu qu'il n'y avait pas différence concernant le taux d'ostéo-intégration entre les différents matériaux implantaires testés. Même si les implants en alumine n'ont pas été considérés comme une alternative viable au titane, la zircone semblait posséder un réel potentiel comme matériel implantaire. Dès lors, de multiples études ont analysé le comportement clinique des

implants en zircone. Le but de ces recherches était d'examiner plusieurs systèmes d'implants dans lesquels le design de l'implant, son état de surface, les protocoles de chirurgie et de mise en charge, la période de suivi et la reconstruction prothétique différaient. En outre, les critères de succès des implants et les indices cliniques variaient d'une étude à l'autre. L'intérêt pour les implants en zircone ne cessent de grandir en témoignent le nombre croissant de systèmes sur le marché ainsi que la forte demande pour des reconstructions non-métalliques et esthétiques. Ainsi, le but de cette revue était d'évaluer d'une part les taux de succès et de survie des implants céramiques en zircone présentant un recul d'au moins une année après leur mise en charge et, d'autre part, de juger en fonction de l'évidence scientifique s'ils peuvent être considérés comme une alternative aux implants en titane.

Cette revue systématique ainsi que cette méta-analyse se sont principalement intéressées aux études cliniques évaluant les taux de survie des implants en zircone un an après leur mise en fonction. En comparaison des revues ultérieures évaluant des études animales ou purement narratives, seules des études cliniques avec un temps d'observation d'un an au minimum avaient été incluses dans cette analyse. Le taux de survie global des implants en zircone était de 92% (95% IC 87-95) après un an de mise en charge, avec une hétérogénéité significative entre les études (I^2=79.3%, tau-squared=0.698, p <0.0001). A titre de comparaison, les taux de survie des implants en titane réhabilités avec une couronne unitaire (SC) étaient de 97.2% à 5 ans et 95.2% à 10 ans *(*16*)*. De même que les taux de survie des implants en titane réhabilités par des ponts fixes (FDP) étaient de 97.2% et 93.1% après 5 et 10 ans, respectivement (17*)*. Néanmoins, en tenant compte du design prothétique, et ainsi en excluant Osman et al. (18) dont le design prothétique était non-conventionnel, l'hétérogénéité entre les études diminua pour atteindre un niveau non-significatif (I^2=41.9%, tau-squared=0.16, p =0.06). En outre, le taux de survie cumulatif des implants en zircone réhabilités par des restaurations fixes augmenta jusqu'à 93% (95% IC 90-95) après un an de mise en charge. Osman et al. (18) avait comparé simultanément des implants en zircone alvéolaires et palatins aux implants en titane utilisés comme piliers pour overdentures. Le taux de survie global était de 71.2% pour le groupe zircone et de 82.1% pour le groupe titane. Ce taux de survie bas était attribué à plusieurs facteurs dont le design des implants en une-pièce et leur surface modérément rugueuse en contact avec la muqueuse, le protocole chirurgical sans lambeau, la distribution non-conventionnelle des implants ainsi que le protocole de mise en charge immédiate. De plus, ces résultats étaient affectés par le taux d'échec élevé des implants palatins (42.1%) probablement dû soit à un traumatisme direct durant le brossage de dents soit à une parafonction de la langue.

Les taux de survie des implants en zircone soutenant des reconstructions fixes s'échelonnaient de 87 à 100%. Cannizzaro et al. (19), qui avait rapporté un taux de survie de 87.5% à un an, avait évalué différents protocoles de mise en charge, et 10 des 40 implants examinés avaient été insérés dans des alvéoles d'extraction. Ceci pouvait expliquer le taux de survie bas de ces implants. De plus, Spies et al. (20), qui avait décrit un taux de 88.9%, avait examiné des implant en zircone renforcé à l'alumine une-pièce. Les trois implants qui ne s'étaient pas ostéo-intégrés faisaient partie des premiers placés. Leur échec précoce était attribué à la temporisation immédiate requise pour les implants une-pièce de même qu'à la période de cicatrisation initiale dépendant de la bonne compliance du patient et de l'expérience clinique du praticien. Cionca et al. (21) rapporta à un taux de survie de 87% pour un système d'implants en deux-pièces. Dans cette étude, un échec primaire avait été

noté alors que cinq autres implants avaient été perdus 1 à 10 mois après leur mise en charge suite au phénomène *«d'aseptic loosening »*. Le design expérimental de l'implant et son traitement de surface avait pu expliquer le taux de survie inférieur à celui d'autres études.

En examinant les modes d'échec des implants en zircone, les implants en une-pièce ont démontré une certaine tendance à l'échec précoce, avec un taux d'échec précoce global de 77% (95% IC 56-90). Cependant, la méta-analyse incluait une étude conduite par Pirker et Kocher (22) qui avait testé deux types d'implants. Tous les six implants du premier groupe présentèrent des échecs précoces, alors qu'un seul sur les douze implants dans le second groupe fut perdu. Ces sept échecs avaient été inclus dans la méta-analyse, ce qui a pu engendrer une confusion dans les résultats. Par ailleurs, seule une étude (23) avait rapporté un taux élevé de fracture avoisinant 11.2% durant une période d'observation de 5.9 années, alors que dans trois autres études (24, 25, 18) les taux de fracture des implants étaient bas, entre 0.8% et 4%. En outre, la seule fracture relatée par Blaschke et al. (24) était due à un traumatisme externe. En ce qui concerne les implants en deux-pièces, deux études (21, 26) ont montré un taux plus élevé d'échec tardif que précoce ainsi que l'absence de fracture d'implants. L'analyse statistique reste dès lors difficile à entreprendre du fait de l'hétérogénéité significative des études et du manque de données sur les implants deux-pièces.

Les résultats de cette analyse doivent être interprétés avec précaution pour différentes raisons. La première, la majorité des études analysées étaient des *« case reports »* présentant un échantillon limité et un suivi à court terme. De plus, les études sélectionnées examinaient des implants en zircone dont le design, les caractéristiques de surface, les protocoles chirurgicaux et les supra-structures prothétiques variaient considérablement. Six études (19, 22, 24, 25, 27, 28) ont rapporté des résultats après implantation immédiate, qui avait déjà démontré des taux de survie significativement plus bas pour les implants en titane (29). En outre, différents types de surface d'implant jouant un rôle prépondérant dans l'ostéo-intégration (30, 31, 33) ont été examinés au travers de ces études. Cette hétérogénéité spécifique pourrait expliquer les différences dans les taux de survie. Parmi les 14 études de cette revue, seul Oliva et al. (28) compara des implants avec différentes modifications de surface. Leur résultat montrait des taux de survie significativement plus élevés pour les implants etchés à l'acide (97.6%) par rapport aux implants rugueux sans ou avec revêtement, 92.77 et 93.57% respectivement. Néanmoins, les données ont pu être compilées puisqu'aucune étude n'utilisait d'implants lisses et qu'il a été démontré que l'utilisation d'implant rugueux permettait une meilleure ostéo-intégration peu importe leur traitement de surface (13, 30, 31, 33, 34, 35). Cependant, combiner les données pour les implants une et deux-pièces était considéré comme l'un des inconvénients de cette analyse. Ceci était inévitable car les études sur les implants en zircone deux-pièces étaient en nombre limité. Les limites des implants une-pièce devaient être aussi prises en

considération. Le manque d'option dans l'angulation des piliers représente une difficulté majeure pouvant compromettre le positionnement chirurgical de l'implant. De même, la préparation des implants devrait être évitée à cause des effets négatifs sur les propriétés physiques du matériau et du manque de donnée sur la stabilité à long-terme de cette manipulation. Les implants en une-pièce exigent également une période de guérison exempte de charge, critère rendu difficile par la présence de forces immédiates de mastication et de la langue appliquées sur leur partie supra-muqueuse (6, 8, 12). Une revue (6) évaluant les implants en zircone une-pièce a montré des taux de survie de 74% à 98% après 12-56 mois, ainsi que des taux de succès variant de 79.6% à 91.6% après 6 à 12 mois de fonction. Toutefois, seul un petit nombre d'études avec des périodes d'observation limité était disponible pour cette analyse. Les implants en zircone deux-pièces ont été introduits afin d'éviter les complications associées aux implants une-pièce, mais leur développement fut ralenti par les propriétés physico-chimiques du matériau. Ainsi, peu d'études cliniques ont évalué les résultats des implants en zircone deux-pièces (21, 25, 26, 36). Il devient dès lors urgent de réaliser d'autres études cliniques sur ce type d'implant.

Une autre limite de cette revue réside dans le type de reconstructions fixes évaluées, du fait que les études sélectionnées examinaient soit des couronnes unitaires ou des ponts scellés. Ceci est attribué au manque de restaurations vissées sur implant en zircone à cause des limitations mécaniques du matériau. Un excès de ciment représente une complication fréquente et sévère dont il a été démontré qu'il peut provoquer une réaction inflammatoire autour des implants en titane (37, 38). Pourtant, aucun cas de péri-implantite associé aux implants en zircone n'a été rapporté. Il reste à déterminer si cette tendance est due à la biocompatibilité de la céramique zircone ou au manque d'études chez l'être humain. Finalement, cette analyse n'a pas abordé le sujet de la perte osseuse marginale, ce qui pourrait être le thème d'une future revue.

En conclusion, malgré le manque d'évidence sur le long terme permettant de justifier leur utilisation, les implants en zircone pourraient représenter une alternative au titane afin de proposer une solution « sans-métal ». Néanmoins, d'autres études cliniques sont nécessaires afin de fournir des résultats à long-terme, et de déterminer les risques de complications techniques et biologiques. Concernant les implants en zircone deux pièces, des études randomisées et contrôlées supplémentaires sont requises afin de comparer leurs taux de survie et de succès avec ceux en titane et en zircone une pièce.

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ENGLISH PART

A systematic review of the clinical survival of zirconia implants

OBJECTIVES

The aim of this review was to evaluate the clinical success and survival rates of zirconia ceramic implants after at least one year of function, and to assess if there is sufficient evidence to justify using them as alternatives to titanium implants

MATERIALS AND METHODS

An electronic search in MEDLINE, EMBASE and the Cochrane Central Register of Controlled Clinical Trials (CENTRAL) databases was performed in April 2015 by two independent examiners to retrieve clinical studies focusing on the survival rate of zirconia implants after at least one year of function. Implant survival was estimated using the overall proportion reported in the studies with a Clopper-Pearson 95% confidence interval (random effect model with a Der-Simonian Laird estimate).

RESULTS

Fourteen articles were selected out of the 1,519 titles initially screened. The overall survival rate of zirconia one- and two-piece implants was calculated at 92% (95% CI 87-95) after one year of function. The overall early failure rate for one-piece zirconia implants was 77% (95% CI 56-90).

CONCLUSIONS

In spite of the unavailability of sufficient long-term evidence to justify using zirconia oral implants, zirconia ceramics could potentially be the successful alternative to titanium for a non-metallic implant solution. However, further clinical studies are required to establish long-term results, and to determine the risk of technical and biological complications. Additional randomized controlled clinical trials examining two-piece zirconia implant systems are also required to assess their survival and success rates in comparison with titanium as well as one-piece zirconia implants.

CLINICAL RELEVANCE

Zirconia implants provide a potential successful alternative to titanium ones.

In a world with increasingly heightened esthetic demand, ceramics have become progressively more popular in the dental industry. Nowadays, they are widely used as veneers and abutments for both tooth- and implant-supported all-ceramic restorations, as well as for fabrication of oral implants. Densely-sintered alumina (Al_2O_3) and yttria-stabilized tetragonal zirconia polycrestal ceramics (Y-TZP) are currently the materials of choice for ceramic abutments [1]. Yet when it comes to oral implants, zirconia has repeatedly been proven superior to other ceramics in terms of bending strength and fracture toughness [2]. Its low modulus of elasticity and thermal conductivity, low affinity to plaque and high biocompatibility, in addition to its white color, have made zirconia a very attractive alternative to titanium in implant dentistry [3-6]. Still, when it comes to disadvantages, low-temperature degradation, also known as ageing, is considered one of zirconia's major drawbacks. It is a process which results in degradation of the mechanical properties due to the progressive spontaneous transformation of the meta-stable tetragonal phase into a monoclinic one at temperatures above 200°C in the presence of water vapor. This causes reduction in the strength, toughness and density of the material. However, reduction in grain size and/or increase in the concentration of stabilizing oxides can reduce the transformation rate [7]. An additional concern when using zirconia oral implants has been addressed in an *in vitro* study evaluating fracture strength. The authors established that both preparation and cyclic loading of zirconia implants can reduce their fracture strength resistance. Nevertheless, they reported that even implants with low mean fracture strength can withstand extended intervals of average occlusal loading [8]. Regardless of the material's physical limitations, animal studies have repeatedly proven zirconia implants to be comparable, if not superior, to titanium implants in terms of biocompatibility and osseointegration [4, 9-14]. A systematic review [12] evaluating the osseointegration of zirconia implants in animal studies demonstrated a mean bone-to-implant contact (BIC) greater than 60% in most of the included studies. Nevertheless, the authors could not recommend the use of zirconia dental implants due to the lack of long term clinical results. Another systematic review [2], which included both animal and clinical studies on alumina and zirconia implants, concluded that there was no difference in the rate of osseointegration between the different implant materials in animal studies. Even though alumina implants were not considered a viable alternative to titanium, zirconia, on the other hand, was viewed as a potential successful implant material in spite of the lack of supporting clinical data. A clinical study further established a lower inflammatory infiltrate and micro vessel density in soft tissues surrounding zirconia healing caps when compared to titanium ones [15].

In view of such encouraging results, multiple clinical studies evaluating the use of zirconia oral implants have been published. Yet different studies examined a variety of implant systems with great diversity in implant design, surface modification, surgical and loading protocols, follow-up period and prosthetic reconstruction. Furthermore, clinical investigations often used variable definitions for implant success with different clinical indexes. Finally, owing to the increasing number of commercially available ceramic implant systems, as well as the increasing demand for non-metallic and highly esthetic restorations, the clinical performance of zirconia implants has become of substantial interest to the dental practitioner. Hence, the aim of this review was to evaluate the clinical success and survival rates of zirconia ceramic implants after at least one year of function, and to assess if there is sufficient evidence to justify using them as alternatives to titanium implants.

The method used in this systematic review was adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16] as well as the recommendations previously established by Needleman [17].

THE FOCUSED QUESTION

The aim of this review is to answer the following focused questions:

1. What are the clinical survival rates of zirconia ceramic implants?
2. Is there sufficient clinical data on zirconia implants to justify using them as alternatives to titanium implants?

SEARCH STRATEGY

An electronic search in MEDLINE, EMBASE and the Cochrane Central Register of Controlled Clinical Trials (CENTRAL) databases was performed for clinical studies published in the English language. No publication year limit was applied so that the search could include the first available year until the first of April 2015. The following search terms (MeSH terms) were utilized: 'dental implants' AND ('zirconium oxide' OR 'yttria-stabilized tetragonal zirconia polycrystals ceramic'), 'dental implants' AND ('zirconia, AND 'clinical study'), 'dental implants' AND ('zirconium oxide'), 'zirconia implants' AND ('clinical' NOT "abutments'), 'zirconia implants' AND ('human study' AND 'survival rate'), as well as 'zirconia implant' AND ('clinical study' AND 'failure rate').

INCLUSION CRITERIA

Publications were considered for inclusion if the following criteria were met:

- Studies reported in the English language in dental journals.
- Clinical studies including at least 5 human subjects with ceramic implant-supported reconstructions.
- All types of zirconia implants including one- and/or two-piece systems.
- Number of implants specified.
- Observation period of at least one year after functional loading.
- Survival and/or success rates clearly stated.
- Clear description of the prosthetic reconstruction.

EXCLUSION CRITERIA

Studies not meeting all inclusion criteria were excluded from the review. Publications based on charts, questionnaires or interviews were also not considered. Due to the limited number of available studies, no further exclusion criteria were specified.

SELECTION OF STUDIES

Titles and abstracts derived from the search were independently screened by two authors, (DH and NC), based on the listed criteria. Full-text articles were then obtained for all titles agreed upon, and disagreements were resolved by discussion. Cohen's kappa was used to measure inter-reviewer agreement.

QUALITY ASSESSMENT

Assessment of the methodological quality of the included studies was done by the two reviewers (DH and NC). The studies where assessed according to their design, extent of clinical and radiographic examinations, adjustment for potential confounding variables and different surgical protocols, completeness of follow-up, and statistical analysis. Industry funding was also taken into consideration. In light of the mentioned criteria, studies were evaluated as having low, moderate or high risk of bias [2, 18].

DATA EXTRACTION

Data was extracted on each study's design, publication year, follow-up period, number of patients and implants, implant design and surface characteristics, surgical protocols, survival and/or success rates, details on marginal bone loss (MBL) and prosthetic rehabilitation, as well as failure and complication rates. Any disagreement regarding data extraction was resolved with discussion. If only failure rates were reported, survival rates were calculated after requesting permission from the authors. When data were not clear, the corresponding author was contacted for clarification.

STATISTICAL ANALYSIS

Statistical heterogeneity, assessed using Chi-square test and I^2 statistics, was used to estimate the proportion of variance due to heterogeneity among studies. The prevalence of survival of implants was estimated using the overall proportion reported in the studies with a Clopper-Pearson 95% confidence interval (random effect model with a Der-Simonian Laird estimate). Forest plots were used to show the prevalence estimated in each study with its confidence interval and the weight given to each study in the meta-analyses along with the overall pooled prevalence.

The initial electronic database search yielded 1,519 titles which were independently screened resulting in the consideration of 43 publications. Abstracts were then reviewed and 4 *in vitro* or animal studies were further excluded. The remaining 39 studies were reviewed in details resulting in the exclusion of 10 articles which were examining the same groups of patients already included in other publications. This was established after email communication with the authors. Both reviewers agreed on the classification of 36 of the 39 studies, with an estimated kappa of 0.84. In case of multiple papers evaluating the same patient group, the latest or the most relevant publications were selected with the exception of Spies et al. [19]. This study evaluated the same group of patients examined in two consecutive publications [20, 21]. In spite of being more recent, the publication of Spies et al. was excluded because it focused on the survival of the prosthetic superstructures that were fabricated using a novel hand-layering technique. Sixteen studies were further excluded due to insufficient sample size or short follow-up period. Finally, 14 clinical trials were selected for inclusion in the current review (Fig.1). Eleven publications examined one-piece implant systems, two evaluated two-piece systems, and one included both one- and two-piece implants. The studies showed variability in implant surface treatment, surgical and loading protocols, prosthetic rehabilitation, and observation period. Hence, meta-analysis was limited to one year of functional loading using a random effect model. Only 3 publications were randomized clinical trials (RCT), whereas the remaining 11 studies where case series with varying designs. Detailed data for the 14 included studies are listed in Table 1.

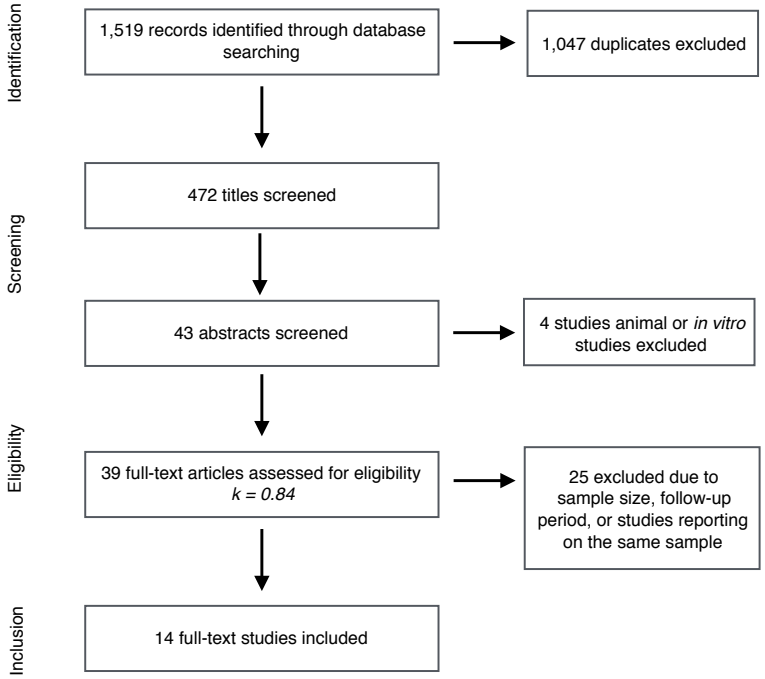

Figure 1: The flow chart for the search strategy

Table 1: Details of the included studies

	Author, year	Study type	Observation period	No. of patients	No. of implants	Implant design	Implant system & surface characteristics	Time & Technique of Implant placement	Type of prosthetic reconstruction and healing time	Survival rate %	Success rate %	Mean MBL (mm)
1	Blaschke & Volz 2006	Prospective	2-5 yrs	34	66	One-piece	Z-Lock 3, VOLZIRKON 1 & 2 (Z-Systems AG, Constance, Germany) CAD/CAM Bio-HIP A Zr, sandblasted intra-osseous section & polished transgingival/ abutment portion	NR	Implants protected during the healing phase by splints or prosthesis, then SC after: Mand: 4 months Max: 6 months	98% good osseointegration after 1-2 years	NR	NR
2	Pirker & Kocher 2009	Prospective	mean 18 months	18	18 Group A: 6 Group B: 12	One-piece	Single-root analogue zirconia implants Group A: Sandblasted Group B: Additional macroretention in interdental space & reduced diameter BL	1-8 days post-extraction by tapping	Immediate limited functional loading Composite SC after 3-13 months	Group A: zero survival in 2 months Group B: 92	NR	NR
3	Oliva 2010	Prospective	mean 40.8 months	378	831 Uncoated (UC) 249 Coated (C) 249 Acid etched (ICE) 333	One-piece	Ceraroot zirconia implants (Oral Iceberg) with 3 different roughened surfaces UC, C, ICE	Immediate, flapless, regeneration, sinus lifts, 1 & 2 stage, or late implant placement, screwed or tapped-in implants	Vacuum stent or immediate provisionally cemented restoration for esthetic areas CAD/CAM final restoration after 4-11 months	Reported success rate only	Overall 94.9 UC 92.77 C 93.57 ICE 97.6	NR
4	Cannizzaro 2010	RCT	12 months	40	40 Occlusal (Occ) 20 Non-occlusal (Non-Occ) 20	One-piece	Z-Look 3 zirconia implants (Z-Systems, Oensingen, Switzerland) with sandblasted surfaces	10 Immediate implant placement (5 Occ, 5 Non-Occ) 30 Late placement	Implant preparation and single immediate acrylic crowns, Occ: immediately occlusally loaded Non-Occ: non-occlusally loaded Ceramic crowns after 4-5 months	Overall 87.5 Occ: 85 Non-Occ: 90	NR	Occ 0.9 ± 0.48 Non-Occ 0.7 ± 0.59
5	Kohal 2012	Prospective case series	12 months	65	66	One-piece	ZiUnite zirconia implants (Nobel Biocare, Gothenburg, Sweden) A machined collar with a roughened transmucosal part, a tapered and roughened endosseous part using a sintering-on technique	Immediate implant placement or in healed sites using flapless, punch or flap techniques	Implant preparation and immediate temporization, then single crowns after: Mand: minimum 6 weeks Max: minimum 14 weeks	95.4	Success criteria (Ostman et al. 2007, 2008) Grade I: 66 Grade II: 86	1.31
6	Kohal 2013	Prospective case series	12 months	28	56	One-piece	ZiUnite zirconia implants (Nobel Biocare, Gothenburg, Sweden) A machined collar with a roughened transmucosal part, a tapered and roughened endosseous part using a sintering-on technique	Immediate implant placement or in healed sites using flapless, punch or flap techniques Bone augmentation without membranes when needed	Implant preparation and immediate temporization, then FDPs after: Mand: minimum 6 weeks Max: minimum 14 weeks	98.2	Success criteria (Ostman et al. 2007, 2008) Grade I: 60 Grade II: 72	1.95
7	Borgonovo 2013	Prospective case series	48 months	13 (10 at follow-up)	35 (28 at follow-up)	One-piece	WhiteSKY zirconia implants (Bredent, Senden, Germany) Sandblasted endosseous surface	Late implant placement with full thickness flap reflection Regenerative procedures used when required	Immediate implant abutment preparation and temporary restorations Final CAD/CAM all ceramic zirconia SC or FDP 6 months after	100	100	1.63
8	Payer 2013	Prospective case series	24 months	20	20	One-piece	WhiteSKY zirconia implants (Bredent, Senden, Germany) sandblasted endosseous surface	Late implant placement with full thickness flap reflection No bone augmentation	Immediate CAD/CAM provisional adhesively cemented restoration (out of occlusion) All ceramic SC after 4 months of healing (provisional ground and used as a cap under the final restoration)	95	95	1.29
9	Osman 2014	RCT	12 months	24 (19 at follow-up) Ti 12 (8 at follow-up) Zr 12 (11 at follow-up)	129 Ti 56 Zr 73	One-piece	Southern Implants (Irene, South Africa) with tapered threaded implant body, a transmucosal cylindrical collar, and a ball abutment Zr: One-piece Zr implants with acid etched surfaces	Late implant placement with full thickness flap reflection except for palatal implants	Implant-supported overdentures 3-4 months after implant placement Maxilla: 2 implants in the premolar regions, 1 off-center and 1 palatal implant Mandible: 2 distal implants in the molar	Overall Zr 71.2 Overall Ti 82.1 Mand. Zr 90.9 Mand. Ti 95.8 Max. Zr 55	NR	Zr 0.42 ± 0.40 Ti 0.18 ± 0.47
10	Payer 2015	RCT	24 months	22	31 Zr 16 Ti 15	Two-piece	Ziterion Vario z, yttria-stablized zirconia implants Ziterion Vario t, titanium implants (Ziterion GmbH, Uffenheim, Germany)	Minimum 6 months healing period	Abutments cemented at 2nd stage surgery under rubber dam isolation 4-6months after implant placement All-ceramic single crowns	Zr 93.3 Ti 100	Zr 93.3 Ti 100	Zr 1.48 ± 1.05 Ti 1.43 ± 0.67
11	Brull 2014	Retrospective	mean 18 months	74	121 Two-piece 66 One-piece 55	One & two-piece	Individually designed implants milled from round, isostatically pressed yttria-stabilized and cerium co-stabilized zirconia blanks, air particle abraded then sintered	Immediate or late placement	Mean healing period 4.6 ± 3-17 months SC: 82.6% FDPs: 17.4%	96.5	NR	0.1 ± 0.6
12	Cionca 2015	Prospective case series	mean 588 ± 174 days	32	49	Two-piece	Zeramex T implants with sandblasted acid-etched surfaces	Late placement in healed sockets	Mean healing period 193 ± 79 days, cemented all ceramic SC	87	NR	NR
13	Spies 2015	Prospective	12 months	27	27	One-piece	Alumina toughened zirconium dioxide ATZ (Ziraldent FR1, Metoxit AG, Thayngen, Switzerland) Zircapore surface (sandblasted with a ceramic slurry coating) Tapered, self-tapping implants with reduced diameter at the transition zone from soft to hard tissues	Late placement in healed sockets	SC immediate provisional restoration then CAD/CAM all ceramic crowns in: mand: 6 weeks Max:14 weeks	88.9	Success criteria (Ostman et al. 2007, 2008) Grade I: 91.7 Grade II: 100	0.77

RCT: Randomized controlled clinical trial. MBL: Marginal bone loss. NR: Not reported. SC: Single crown. FDP: Fixed dental prosthesis. Mand: Mandible. Max: Maxilla. CAD/CAM: Computer-aided design/Computer-aided manufacturing. Zr: Zirconia implants. Ti: Titanium implants. UC: Uncoated implant surfaces. C: Coated implant surfaces with Na_2O-K_2O-MgO-Al_2O_3-CaO-SiO_2-P_2O_5-F. ICE: Acid etched implant surfaces. Success grade I (Ostman et al. 2007): Implants with no clinical or radiographic signs of pathology, showing ≤ 2 mm bone resorption at the 1-year follow-up. Success grade II (Ostman et al. 2007): Implants with no clinical or radiographic signs of pathology, showing ≤ 3 mm bone resorption at the 1-year follow-up.

Cont. Table 1

	Author, year	Study type	Observation period	No. of patients	No. of implants	Implant design	Implant system & surface characteristics	Time & Technique of Implant placement	Type of prosthetic reconstruction and healing time	Survival rate %	Success rate %	Mean MBL (mm)
14	Roehling 2015	Retrospective	mean 5.94 ± 0.09 yrs	71	161 3.25mm diameter 51 (31.7%) 4.0mm diameter 82 (50.9%) 5.0mm diameter 28 (17.4%)	One-piece	Z-Look 3 (Z-Systems GmbH, Kiel, Germany) with sandblasted surfaces	At least 6 weeks post-extraction	At least 3 months healing period (Implants immediately protected from premature loading) SC 69% FDP 19.3% Removable hybrid dentures 2.5%	Overall 77.3 3.25mm implants 58.5 4.0mm implants 88.9 5.0mm implants 78.6	Overall 77.6 3.25mm implants 58.8 4.0mm implants 89 5.0mm implants 78.6	0.97 ± 0.07

RCT: Randomized controlled clinical trial. MBL: Marginal bone loss. NR: Not reported. SC: Single crown. FDP: Fixed dental prosthesis. Mand: Mandible. Max: Maxilla. CAD/CAM: Computer-aided design/Computer-aided manufacturing. Zr: Zirconia implants. Ti: Titanium implants. UC: Uncoated implant surfaces. C: Coated implant surfaces with Na_2O-K_2O-MgO-Al_2O_3-CaO-SiO_2-P_2O_5-F. ICE: Acid etched implant surfaces. Success grade I (Ostman et al. 2007): Implants with no clinical or radiographic signs of pathology, showing ≤ 2 mm bone resorption at the 1-year follow-up. Success grade II (Ostman et al. 2007): Implants with no clinical or radiographic signs of pathology, showing ≤ 3 mm bone resorption at the 1-year follow-up.

EXCLUDED STUDIES

Out of the 39 publications reviewed in details, 25 were excluded from the final analysis (Table 2). The main reasons for exclusion were:

- Sample size.
- Observation period of less than one year after loading.
- Unclear surgical and/or prosthetic protocol.
- Studies examining the same group of patients.

Table 2: Excluded studies and reasons for exclusion

	Author, year	Reason for exclusion
1	Kohal 2004	Sample size
2	Oliva 2007	The same group of patients included in Oliva 2010
3	Oliva 2008	Sample size
4	Oliva 2008, 2	Sample size
5	Pirker & Kocher 2008	Sample size
6	Oliva 2010, 2	Sample size
7	Walker 2010	Sample size
8	Borgonovo 2010	The same group of patients included in Borgonovo 2014
9	Arnetzl 2010	Sample size
10	Nevins 2011	Sample size
11	Pirker 2011	Sample size
12	Borgonovo 2011	The same group of patients included in Borgonovo 2014
13	Borgonovo 2012	The same group of patients included in Borgonovo 2014
14	Pirker & Kocher 2012	Sample size
15	Oliva 2012	Titanium implants with zirconia superstructures
16	Borgonovo 2013	The same group of patients included in Borgonovo 2014
17	Borgonovo 2013, 2	The same group of patients included in Borgonovo 2014
18	Osman 2013	Sample size
19	Gahlert 2013	The same group of patients included in Roehling 2015
20	Aydin 2013	Sample size
21	Nair 2013	Sample size
22	Bankoglu 2014	Sample size
23	Spies 2014	The same group of patients included in Kohal 2012, 2013 but this study evaluated the survival of prosthetic superstructures
24	Siddiqi 2015	The same group of patients included in Osman 2014
25	Gahlert 2015	Functional loading period less than 1 year

QUALITY ASSESSMENT

Table 3 shows the list of studies detailing the criteria used for quality assessment. One study [22] was considered highly biased due to unavailability of details on neither clinical nor radiologic examinations, lack of adjustment for different surgical protocols and lack of statistical analysis. Six articles [20, 21, 23-26] were considered to have a moderate degree of bias, while the remaining seven [27-33] studies had a low degree of bias.

Table 3: Quality assessment of the included studies

	Study ID	Design	Evidence level*	Detailed clinical exam	Rx: quality and interpretation	Adjustment for different surgical and loading protocols	Completeness of follow-up	Statistical analysis	Industry Funding	Risk of Bias
1	Blaschke 2006	Prospective	III	No	No	No	Yes	No	Yes	High
2	Pirker & Kocher 2009	Prospective	III	Yes	No	No	Yes	Yes	Unclear	Moderate
3	Cannizzaro 2010	RCT	Ib	No	Yes	Yes	Yes	Yes	Yes	Low
4	Oliva 2010	Prospective	III	No	No	Yes	Yes	Yes	Unclear	Moderate
5	Kohal 2012	Prospective case series	III	Yes	Yes	No	Yes	Yes	Yes	Moderate
6	Kohal 2013	Prospective case series	III	Yes	Yes	No	Yes	Yes	Yes	Moderate
7	Borgonovo 2013	Prospective	III	Yes	Yes	Unclear	Yes	Yes	No	Low
8	Payer 2013	Prospective case series	III	Yes	Yes	Yes	Yes	Yes	Yes	Low
9	Osman 2013	RCT	Ib	No	Yes	No	Yes	Yes	Unclear	Moderate
10	Payer 2015	RCT	Ib	Yes	Yes	Yes	Yes	Yes	Yes	Low
11	Cionca 2015	Prospective case series	III	Yes	No	Yes	Yes	Yes	Yes	Low
12	Brull 2014	Retrospective	III	Yes	Yes	No	Yes	Yes	Yes	Moderate
13	Spies 2015	Prospective	III	Yes	Yes	Yes	Yes	Yes	Yes	Low
14	Roehling 2015	Retrospective	III	Yes	Yes	Yes	Yes	Yes	No	Low

* According to the definitions of types of evidence originating from the US Agency for Health Care Policy and Research (1993)

ASSESSMENT OF HETEROGENEITY AND META-ANALYSIS

Preliminary examination of the survival of implants at one year for the selected studies revealed considerable heterogeneity, (I^2=79.3%, tau−squared=0.698, $p < 0.0001$). Information on each study's characteristics are detailed in Table 1.

DESCRIPTION OF INCLUDED STUDIES

One-Piece Implants

Eleven studies evaluated one-piece implant systems and one included both one- and two-piece implants. Of these, five investigations examined both immediate and late implant placement and one did not report the timing of implant surgery.

In the first study [22], 34 patients with 66 zirconia implants were monitored over a period of two to five years. The fixtures were either splinted or protected with special prostheses during a healing period of 4 to 6 months. However, details regarding timing, surgical protocol, clinical and radiographic examinations were not provided. The authors reported good osseointegration related to 98% of the implants one to two years following implantation. Only one implant was fractured due to external trauma and thereby extracted and subjected to histological evaluation. This revealed direct BIC with neither a fibrous layer nor signs of a foreign body reaction.

Another study [23] evaluated immediate, non-submerged, root-analogue zirconia implants with two different surfaces for single-rooted tooth replacement. Six patients received root-identical replicas with sandblasted implant surfaces, while 12 patients received modified implants with added interdental macro-retention and a slightly reduced bucco-lingual dimension. Implants were inserted one to eight days after tooth extraction by tapping, which resulted in immediate limited functional loading. All 6 implants in the first group failed prior to prosthetic restoration. The 12 patients in the second group received single composite crowns after a healing period of 3 to 5 months. The overall survival rate of the modified implants was 92% after 1-33 months of function. The authors reported excellent esthetic and functional results with minimal bone resorption and soft tissue recession.

A third study [24] evaluated the 5-year success rate of 831 zirconia implants with three different surfaces: uncoated (UC, n=249), coated (C, n=249), and acid-etched (ICE, n=333). The UC implants were roughened by mechanical grinding, while the C implants were roughened and coated with a bioactive ceramic coating composed of Na_2O-K_2O-MgO-Al_2O_3-CaO-SiO_2-P_2O_5-F, then sintered. This investigation included immediate as well as late implant placement with or without simultaneous bone augmentation, as well as one- or two-stage sinus lifts. Three-hundred-seventy-eight patients with a mean follow-up period of 3.4 years were examined. The overall 5-year success rate was 95%, with ICE implants showing significantly higher success rate compared to both the UC and C ones.

A multi-center randomized controlled clinical trial [27] further compared 20 single non-occlusally loaded zirconia implants with 20 occlusally loaded implants after one year of function. Five implants in each group were placed in fresh extraction sockets. Overall, five implants (12.5%) failed early; four of which were immediately placed after tooth extraction, and three were occlusally loaded. Both occlusal and non-occlusal implants showed significant marginal bone loss after one year of loading but the difference was not statistically significant between groups. The authors concluded that there was an association between immediate implants and implant failure.

Another group investigated one-piece zirconia implants for single-tooth replacement or fixed dental prosthesis (FDP) in two consecutive publications. The first [20] included 65 patients treated with 66 single one-stage implants and immediate temporization. Five implants (9%) were placed in fresh extraction sites, 19 (27%) were placed in healed sites using a flapless technique, and 42 (64%) were placed after flap elevation. Three implants failed early prior to prosthetic restoration leading to a cumulative survival rate of 95.4% after one year. A mean marginal bone loss (MBL) of 1.31 mm was reported, with 19 implants (34%) losing at least 2 mm of bone, and 8 (14%) losing more than 3 mm of marginal bone. Yet stable and healthy peri-implant soft tissue conditions were noted at the one year follow-up. Regardless, the authors could not recommend the use of the tested implant system in clinical practice.

The second publication [21] evaluated the one year results of 3-unit FDPs in 28 patients with 56 implants. Five implants (9%) were immediately placed (2 after flap elevation), 51 implants were placed in healed sites (5 using the punch technique and 2 flapless). Only one implant belonging to the immediately placed group failed prior to prosthetic reconstruction, resulting in a survival rate of 98.2% after one year. The mean MBL was 1.95 mm after one year. However, 10 patients (40%) showed at least 2 mm of MBL, while 7 (28%) lost more than 3 mm, and 3 (12%) lost more than 4 mm of marginal bone. A correlation was found between MBL and the flap design. Implants placed using a flapless approach or the punch technique showed significantly more MBL than those placed after flap elevation. Finally, due to the high frequency and increase in radiographic bone loss around the tested implants, the authors concluded that this one-piece zirconia implant system might perform inferiorly to conventional titanium implant systems and to other zirconia implants in terms of MBL.

A 4-year clinical and radiographic study [28] evaluated 13 patients with 35 zirconia implants placed in healed sites. Twenty implants were used for multiple teeth replacement while the rest replaced single teeth. However, only 10 patients with 28 implants were available for the final examination. Success and survival rates were calculated at 100% after 48 months. The mean MBL was 1.631 mm at the end of the follow-up period, with maxillary implants showing significantly higher MBL during the first year of loading when compared to mandibular ones. In contrast, no differences in MBL were found between implants restored with single crowns (SC) or FDP. Finally, the authors stated that minimal plaque

accumulation, no bleeding, and PD of 3.19 mm could be expected around zirconia implant-supported restorations.

Another prospective case series [29] evaluated the outcomes of 20 single-piece, immediately provisionalized, zirconia implants placed in single-tooth gaps after a period of 2 years. The results showed 95% survival and success rates with a mean MBL of 1.29 mm at the end of the observation period. Clinical parameters showed healthy soft tissue conditions and an improved, but not significant, pink esthetic score [34] after 24 months. Regardless of such promising results, the authors refrained from drawing final conclusions or clinical recommendations.

One-piece zirconia implants were also evaluated as abutments supporting overdentures in comparison with titanium implants of similar design [26]. This randomised controlled clinical trial included 24 edentulous patients with 129 implants randomly divided into two groups: the zirconia test group and the titanium control group. Each participant received 4 maxillary implants distributed in a diamond-shaped quad design (1 mid-palatal and 3 anterior crestal), and 3 mandibular implants with a tripod design (1 mid-symphyseal and 2 bilateral distal). There was no significant difference in the survival rate between the groups, but the overall survival rate of 71.2% was considered low in comparison with other zirconia implant trials. Regarding mandibular implants, the survival rate of the titanium group was 95.8% compared to 90.9% for zirconia implants. The maxillary implants' survival rates were 71.9% and 55% for the titanium and zirconia implants, respectively. Statistical analysis showed a significantly higher risk of failure for maxillary implants. The mean MBL was 0.18 mm for titanium and 0.42 mm for zirconia implants for both jaws combined. In contrast to implants placed in the upper arch, significantly higher MBL was found around zirconia implants placed in the mandible when compared to the titanium group. Moreover, three zirconia implants fractured, two of which were located in the maxillary jaw, resulting in the recommendation of at least four wider diameter fixtures for maxillary overdenture support when using zirconia implants. Further modifications of implant design to improve biomechanics integrity was also recommended. Finally, the authors advised for caution before recommending the use of single-piece zirconia implants for overdenture support.

A more recent prospective investigation [33] was conducted to determine the clinical and radiographic outcomes of one-piece alumina-toughened zirconia implants for single-tooth replacement in 27 patients. Three implants were lost early prior to prosthetic reconstruction. Hence, 24 patients were seen at the one-year follow-up, resulting in a survival rate of 88.9%. The mean MBL was 0.77 mm at follow-up, with only two implants (8.3%) losing at least 2 mm of bone. Probing depth (PD) and calculated attachment level (CAL) increased while recession remained stable during the observation period. Mean bleeding (mBI) and plaque (mPI) indexes showed no statistically significant changes within the first year. The

authors finally concluded that the tested implant system showed promising short-term results and seemed to be a candidate for clinical use.

Another recent study [32] examined zirconia one-piece implants after up to 7 years of loading. A total of 71 patients with 161 implants and a mean follow-up period of 5.94 years were included in this analysis. The overall survival rate was 77.3%. Implants with reduced diameter (3.25 mm) showed the lowest survival rate at 58.5% in comparison with implants of 4.0 mm and 5.0 mm diameter at 88.9% and 78.6%, respectively. Fourteen implants were lost prior to prosthetic reconstruction, 4 failed late, and 18 implants were fractured at the coronal part of the sandblasted implant body. The authors concluded that the first-generation zirconia implants investigated showed low overall survival and success rates. They also noted that non-fractured failures were not associated with peri-implant infections.

Two-piece Implants

Only two clinical studies evaluating two-piece zirconia implants were included in the current analysis. The first was a prospective study [30] that included 32 patients treated with 49 implants supporting single crowns. The cumulative survival rate was 87% after one year of loading. All failures were due to aseptic loosening. Furthermore, the authors reported no soft tissue complications nor MBL exceeding 2 mm at the end of the observation period.

The second study was a randomized clinical trial [31] that evaluated 16 zirconia implants in comparison with 15 titanium implants of identical shape in 22 patients. After up to two years of loading, the survival rate was 93.3% and 100% for zirconia and titanium implants, respectively. The mean MBL was 1.48 mm for zirconia and 1.43 mm for titanium. The authors further concluded that zirconia implants' survival rate and clinical outcomes showed no significant differences in comparison with titanium implants.

One study [25] retrospectively analyzed the clinical performance of both one and two-piece implants in 74 participants over a period of three years. A hundred-twenty-one implants (55 one-piece and 66 two-piece) were evaluated after a mean observation period of 18 months. The cumulative survival rate of 96.5% was calculated after three years, and the surviving implants showed healthy mucosal conditions with significantly lower BOP and PPD around implants when compared to teeth.

IMPLANT SURVIVAL

All but two studies reported cumulative survival rates after at least one year of loading. Cannizzaro et al. reported failure rates which were used for calculation of the survival rate after requesting the author's permission [27]. On the other hand, the one-year survival rate could not be extrapolated for the study conducted by Bull et al. who reported the three-year survival rate of both one- and two-piece implants [25]. Therefore, this study was excluded from the quantitative analysis. Only one study reported survival of one-piece implants after 4 years [28], while two others reported the cumulative survival rates after 5 [24] and 7 years [32]. Yet the meta-analysis was limited to survival of implants at one year due to the limited observation period in most studies. The overall survival rate of zirconia one- and two-piece implants was 92% (95% CI 87-95) after one year of function (Fig. 2).

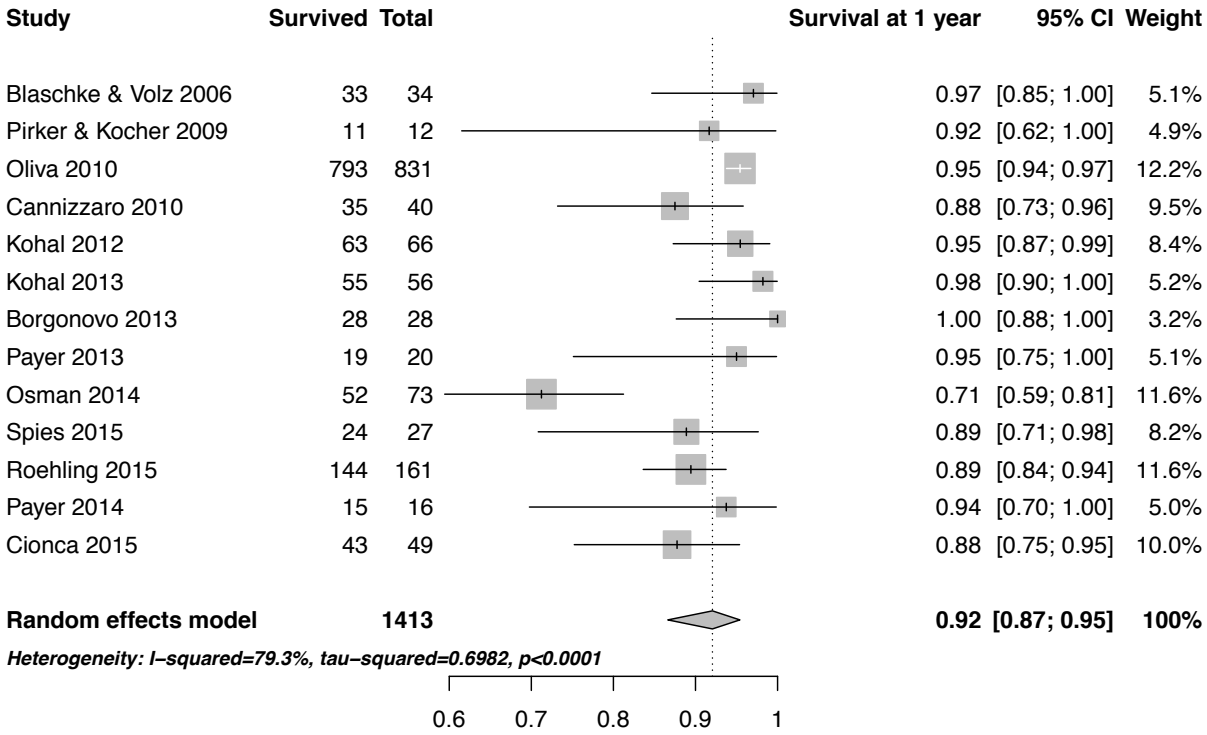

Figure 2: Forest plot for the survival of zirconia implants after 1 year of function when all selected studies were included except Brull et al. [25]

Table 4 shows the prevalence of early and late failures across the studies and Figure 3 shows the forest plot for the early failures of one-piece zirconia implants. However, the meta-analysis was done on one-piece implants excluding Borgonovo et al. [28] who presented data on 28 surviving implants after 4 years of function and hence no failures were reported in this publication. Early failure of one-piece zirconia implants ranged between 1.8% [21] and 100% [23], with the overall early failure rate calculated at 77% (95% CI 56-90). On the other hand, only two [30, 31] out of the three studies evaluating two-piece zirconia implants clearly reported failure rates. Cionca et al. reported a failure rate of 12.2% with only 1 early failure (2%) compared to 5 (10.2%) late failures [30]. Payer et al. showed a 6.3% failure rate with only one implant failing after prosthetic rehabilitation [31]. In contrast,

Brull et al. [25] who examined both one- and two-piece implants, only reported the loss of 3 implants (1 early failure, 1 late failure and 1 fractured implant) without details on the implant design. Thus, meta-analysis could not be performed on the early failure of two-piece implants.

Table 4: Failure rate and prevalence of early failure, late failure and implant fracture in the included studies

	Author, year	Observation period	N of implants	Calculated failure rate %	N of early failures (%)	N of late failures (%)	N of fractured implants (%)
One-piece implants							
1	Blaschke & Volz 2006	2-5 years	34	2%	1 (2.9%)	0	1 (2.9%)
2	Pirker & Kocher 2009	mean 18 months	Group A: 6	Group A: 100%	Group A: 6 (100%)	0	0
			Group B: 12	Group B: 8%	Group B: 1 (8.3%)	0	0
3	Oliva 2010	mean 40.8 months	831	5.05%	38 (4.6%)	4 (0.5%)	0
4	Cannizzaro 2010	12 months	40	12.5%	5 (12.5%) 3 occlusal, 2 non-occlusal	0	0
5	Kohal 2012	12 months	66	4.6%	3 (4.6%)	0	0
6	Kohal 2013	12 months	56	1.8%	1 (1.8%)	0	0
7	Borgonovo 2013	48 months	28	0%	0	0	0
8	Payer 2013	24 months	20	5%	1 (5%)	0	0
9	Osman 2014	12 months	73	28.7%	15 (20.6%)	3 (4.1%)	3 (4.1%)
10	Spies 2015	12 months	27	11.1%	3 (11.1%)	0	0
11	Roehling 2015	mean 5.94 years	161	22.4%	14 (8.7%)	4 (2.5%)	18 (11.2%)
Two-piece implants							
1	Payer 2015	24 months	16	6.3%	0	1 (6.3%)	0
2	Cionca 2015	mean 588 days	49	12.2%	1 (2%)	5 (10.2%)	0
One & two-piece implants							
1	Brull 2014	mean 18 months	121	2.5%	1 (0.8%)	1 (0.8%)	1 (0.8%)

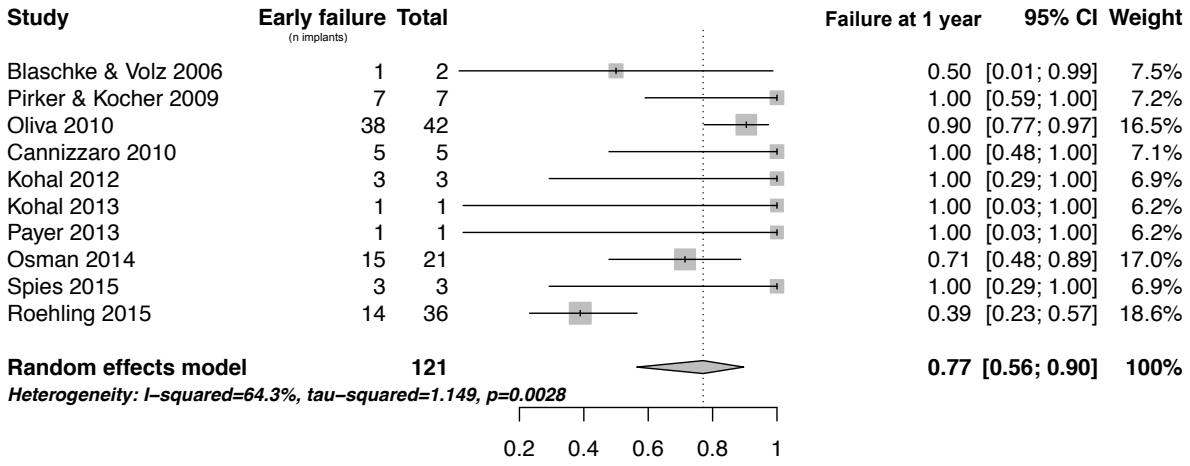

Figure 3: Forest plot for the early failure of zirconia one-piece implants where only the studies evaluating one-piece implants were included with the exception of Borgonovo et al. [28] and Brull et al. [25]

This systematic review and meta-analysis focused on clinical studies evaluating the survival rate of zirconia implants after one year of function. In contrast to previous reviews, which either evaluated animal studies or were only narrative, only clinical studies with an observation period of at least one year were included in this analysis. The overall survival rate of zirconia implants was 92% (95% CI 87-95) after one year of function. In comparison, the overall survival rates of titanium implants supporting single crowns (SC) were 97.2% at 5 years, and 95.2% at 10 years [35]. While the survival rates of titanium implants supporting fixed dental prosthesis (FDP) were 97.2% and 93.1% after 5 and 10 years, respectively [36]. Yet when the prosthetic design is taken into consideration, thereby excluding Osman et al. [26] due to their unconventional prosthetic design, the heterogeneity between the studies decreased to an insignificant level (I^2=41.9%, tau−squared=0.16, p=0.06). Moreover, the cumulative survival rate for zirconia implants with fixed reconstructions increased to 93% (95% CI 90-95) after one year of function (Fig. 4). Osman et al. compared both alveolar and palatal zirconia implants to titanium ones as abutments for overdentures. The overall survival rate was 71.2% for zirconia and 82.1% for titanium implants. This generally low survival was attributed to the implants' one-piece design and their moderately rough surface being in contact with the mucosa, as well as the flapless surgical protocol, the unconventional distribution of the implants, and the immediate loading protocol. Furthermore, their results were affected by the high failure rate of mid-palatal implants (42.1%), which was believed to be due to either direct trauma from tooth brushing or parafunctional tongue activity.

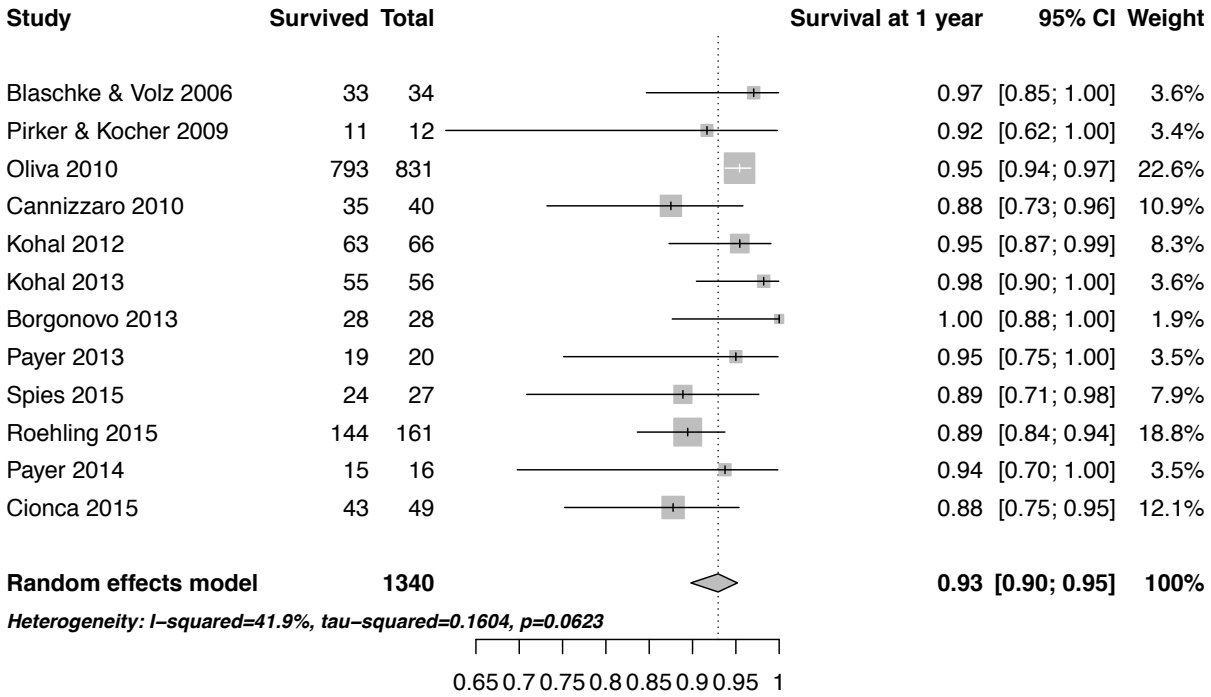

Figure 4: Forest plot for the survival of zirconia implants after 1 year of function excluding Osman et al. [26] and Brull et al. [25]

The survival rates for zirconia implant-supported fixed reconstructions ranged from 87% up to 100%. Yet Cannizzaro et al. [27] who reported a survival of 87.5% at one year, evaluated different loading protocols (immediate occlusal or non-occlusal), and 10 out of the 40 implants examined were inserted into fresh extraction sockets. This could account for the lower survival rate of their implants. Moreover, Spies et al. [33], who reported a survival of 88.9% at one year, examined one-piece alumina-toughened zirconia implants. The three implants that failed to osseointegrate were among the first inserted, and their early failure was attributed to the immediate temporization required for one-piece implants and the initial healing period that is highly dependant on the patient's good compliance as well as the clinician's practical values. Cionca et al. [30] further reported a survival rate of 87% for a two-piece implant system with an acid-etched sandblasted surface. In this study, only one implant failed to osseointegrate while five others were lost one to ten months after loading due to aseptic loosening. The implants' experimental design and the type of surface treatment used could have contributed to the lower survival rate when compared to other studies.

When the failure patterns of zirconia implants were examined, one-piece zirconia implants demonstrated a higher tendency towards early failure (Table 4 and Fig. 3), with the overall early failure rate calculated at 77% (95% CI 56-90). However, the meta-analysis included a study conducted by Pirker and Kocher which included two types of implants. All six implants in the first group failed early while only one out of the 12 implants in the second group was lost. Still, the seven reported failures were included in the meta-analysis of the early failure which could have confounded the results [23]. Furthermore, only one study [32] reported a high fracture rate of 11.2% during a mean observation period of 5.9 years, while three others [22, 25, 26] reported low implant fracture rates ranging between 0.8% and 4%. Moreover, the single fracture reported by Blaschke et al. was due to external trauma [22]. On the other hand, the two studies examining two-piece implants [30, 31] reported a higher percentage of late compared to early failure, and no fractured implants (Table 4). Yet, the significant heterogeneity of the studies and the scarcity of data on two-piece implants hindered statistical analysis.

The results of this analysis should be interpreted with caution for several reasons. First, the majority of the analyzed studies were case reports with limited sample size and short-term follow-up. Second, the selected studies examined zirconia implants with considerable variability in implant design, surface characteristics, surgical protocols and prosthetic superstructures. Six studies reported on outcomes after immediate implant placement [20, 21, 23-25, 27], which has been proven to have significantly lower survival rates for titanium implants [37]. Furthermore, the heterogeneity between studies regarding the type of implant surface treatment, which significantly affects osseointegration [38-40], could account for the differences in survival rates. Of the studies included in this investigation, only Oliva et al. compared implants with different surface modifications. They established that acid-etched

zirconia implants had significantly higher survival rates (97.6%) when compared to the simply roughened uncoated or coated implants, at 92.77% and 93.57%, respectively [24]. Comparison of a certain type of surface treatment across studies could not be done due to the high variability between studies in that respect. However, since none of the studies utilized machined implants, and since multiple studies showed better osseointegration of roughened zirconia implants in spite of the surface treatment used [13, 38, 39, 41-43], pooling the data was considered appropriate. However, combining the data from one- and two-piece implant systems was still considered one of the downsides of this analysis. This was unavoidable due to the scarcity of reports on two-piece zirconia implants. Also, limitations of one-piece implant systems should be taken into consideration. The sparse options for abutment angulation presents a major difficulty that could compromise the surgical positioning of the implant. Furthermore, preparation of sub-optimally positioned implants should be avoided due to its adverse effects on the material's physical properties, as well as the lack of data on the long-term stability afterwards. Single-piece implants also require a load-free healing period, which could be challenging due to the inevitable immediate forces directed at the supra-mucosal part during mastication or with tongue movement [6, 8, 12]. A review [6] evaluating one-piece zirconia implants showed survival rates ranging from 74 up to 98% after 12-56 months, with success rates varying between 79.6% and 91.6% after 6-12 months of function. However, a small number of studies with limited observation periods were available for this analysis. Two-piece zirconia implants were introduced to overcome complications associated with one-piece systems, but their development of has been hindered by the material's physical properties, and only few clinical studies evaluated the outcomes of zirconia two-piece implants [25, 30, 31, 44]. This sheds light on the urgent need for further studies examining such implants.

An additional drawback to this review was the type of fixed reconstructions evaluated, as all selected studies examined cemented SCs or FDPs. This was attributed to the lack of screw-retained zirconia implant-supported restorations due to the material's physical limitations. However, excess cement presents a frequent and major complication that has been proven to provoke an inflammatory reaction around titanium implants [45, 46]. Yet, incidence of peri-implantitis has never been reported in conjunction with zirconia implants. It remains to be determined wether this is due to the higher biocompatibility of zirconia ceramics or if it is merely due to the lack of studies on the subject. Finally, this analysis did not address the high MBL associated with zirconia implants, which could be the focus of a future review.

CONCLUSIONS

Despite the unavailability of sufficient long-term evidence to justify using zirconia oral implants, zirconia ceramics could potentially be the successful alternative to titanium for a non-metallic implant solution. However, further clinical studies are required to establish long-term results, and to determine the risk of technical and biological complications. Finally, additional RCTs examining two-piece zirconia implant systems are required to assess their survival and success rates in comparison with titanium as well as one-piece zirconia implants.

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