

Clinical Oral Investigations

Seven-year prospective clinical study on zirconia based single crowns and fixed dental prostheses --Manuscript Draft--

Manuscript Number:	CLOI-D-13-00900R2
Full Title:	Seven-year prospective clinical study on zirconia based single crowns and fixed dental prostheses
Article Type:	Original Article
Corresponding Author:	chiarella sforza, MD univ milano milano, mi ITALY
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	univ milano
Corresponding Author's Secondary Institution:	
First Author:	gianluca martino tartaglia
First Author Secondary Information:	
Order of Authors:	gianluca martino tartaglia ernesto sidoti chiarella sforza, MD
Order of Authors Secondary Information:	
Abstract:	<p>Objectives. Zirconia based prostheses are used for aesthetic crown and fixed restorations, but follow ups are still limited. The authors evaluated the 7-year clinical results of 303 zirconia core restorations, performed in a general dental private practice.</p> <p>Materials and Methods. Clinical events (fracture and loss of retention, gingivitis, tenderness, excess cement, temporary pain) were recorded in 303 zirconia core restorations positioned in 88 patients. Kaplan-Meier survival probability estimates were computed for failures (needed the replacement or removal of the prosthesis) and complications (resolved without replacing the prosthesis).</p> <p>Results. One hundred and fifty single crowns (130 tooth-supported, 20 implant-supported) and 153 multiple units up to 6 elements (49 tooth-supported, 104 implant-supported) were followed up for 7 years in 88 patients (40 men, 48 women), aged 35-89 years (mean 57). During the follow-up period, there were no complications for 287 (95%) of the restorations. Sixteen restorations/abutment teeth (5%) had some complication: extraction of abutment tooth (7; 2%); caries (2; 1%), porcelain veneer fracture (3; 1%), loss of retention (4; 1%). Nine (3%) restorations were recorded as failures. The overall 7-year survival probability estimate for failures was 0.966 (95% confidence limits, 0.932 and 0.983), for complications was 0.976 (95% confidence limits 0.947 and 0.989), with a cumulative survival rate of 94.7%</p> <p>Conclusions. Within the analysed follow-up, zirconia core restorations appear a good clinical solution, with favourable functional properties.</p> <p>Clinical Relevance. All ceramic restorations can be successfully used for both single and multiple unit prostheses, either teeth or and implants supported.</p>
Response to Reviewers:	<p>Dr Gottfried Schmalz Editor-in-Chief Clinical Oral Investigations</p> <p>Milano, 7 June 2014</p> <p>Dear dr Schmalz, Please find enclosed the revised version of our MS #CLOI-S-13-01155R1 "Seven-year prospective clinical study on zirconia based single crowns and fixed dental prostheses" by Gianluca M. Tartaglia, Ernesto Sidoti, and Chiarella Sforza.</p>

Thank you very much for your consideration of our manuscript; we appreciate the opportunity to resubmit our article, subject to adequate revision and response to the comments raised by the reviewers.

We revised the paper by modifying the Abstract, Methods, and Discussion sections based on the helpful comments. As asked, we list point by point our responses to the questions raised by the reviewers. Additionally, the modified text is highlighted in yellow in the MS.

We would like to thank the reviewers who identified areas of the manuscript that needed modification and also thank you for allowing us to improve the content of the paper.

We trust that the present version of the MS will be suitable for publication in Clinical Oral Investigations.

Sincerely,

Prof. Chiarella Sforza
Dipartimento di Scienze Biomediche per la Salute - via Mangiagalli 31
I-20133 MILANO – ITALY
Tel. +39 02 503 15407
Fax +39 02 503 15387
e-mail chiarella.sforza@unimi.it

Reply to reviewer # 1

1. Concern of the reviewer:

The reviewer agrees with all revisions, except the revision related to comment 7, which was related to the comment:

Because glass-ionomer cement was used for final cementation the authors should give some explanation for the relatively low incidence of loss of retention in their study. Especially beyond the background, that in the study of Rinke et al. 2013 concluded that conventional cementation led to an increased rate of loss of retention and is considered as a critical factor.

Please remove the sentence „Clinically, a key-role of the frictional resistance between the abutment and the crown should be recognized." because this could be misinterpreted, that all-ceramic crowns should be fabricated with an active fit to generate a mechanical friction. Since active mechanical friction would result in tensile stresses within the internal surface area of the restoration, a high risk of flaw initiation will be involved. In contrast a passive fit, without any mechanical friction would be advantageous for all-ceramic restorations, which should be combined with an adhesive insertion to avoid the risk of loss of retention.

Our response: We removed the sentence as suggested.

Revised text: not applicable.

Reply to reviewer # 2

Concern of the reviewer:

1. Please define clearly and briefly in the abstract what was regarded as failure and what as complication (as you did in math and meth).

Our response: done as suggested

Revised text: Kaplan-Meier survival probability estimates were computed for failures (needed the replacement or removal of the prosthesis) and complications (resolved without replacing the prosthesis).

Concern of the reviewer:

2. The fracture toughness of zirconia is approximately 10 times lower than the fracture toughness of a precious alloy for large span PFM-FDPs. The authors do not need to address to that remark.....

Our response: thank you for the technical note.

Revised text: not applicable.

Concern of the reviewer:

3a. The authors wrote: "Tooth supported prostheses were used only on root- or teeth with endodontic revision." Please revise the wording of the sentence. The authors surely mean "root canal treated teeth and teeth with successful endodontic revision"!

Our response: thank you for the helpful suggestion, the text was revised

Revised text: Tooth supported prostheses were used only on root canal treated teeth

and teeth with successful endodontic revision.

Concern of the reviewer:

3b. Again the question rises, if e. g. in a six unit FDP all supporting abutment teeth had to be root canal treated. According to the authors' statement that should be fact. Please explain. Sorry for being that obtuse and insistent - but the reviewer still holds the opinion that this is important - e. g. it is easier to keep recommended thicknesses easier on RCT teeth than on vital ones! On the other hand a lower sensitivity to perceive bite forces is discussed for RCT teeth. This would increase the risk of chippings.....

Our response: multiple units FDPs were a clinical choice imposed, if we had to restore a partially edentulous space (prosthesis without cantilever and rules design indicated in the paper), or suggested for limited occlusal residual space during simulated excursion of the mandible. E.g., if during the simulated movements of the mandible the recommended thickness (zirconia + ceramic) was considered limited, without the possibility to modify the abutment dimensions, we apply a multiple unit FDPs option instead of single units. We perfectly agree with your considerations about RCT teeth.

Revised text: not applicable.

Concern of the reviewer:

4. "no age differences": no age difference between what?

Our response: the text was modified to avoid any misunderstanding.

Revised text: no age differences between men and women.

Concern of the reviewer:

5. Failure rate and complication rate analysis: As far as the reviewer understood still complications (without the necessity of removal) and the failure rate (removal of the restoration) are still separated into different calculations. Normally the failures are a component of the complication as they are severe complications.

Our response: we followed the papers by Burke (J Dent 41:992-999, 2013) and (Ortorp J Dent 40:527-530, 2012), as specified in MM.

Revised text: not applicable.

Seven-year prospective clinical study on zirconia based single crowns and fixed dental prostheses

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

Gianluca M. Tartaglia^{1,2}, Ernesto Sidoti², and Chiarella Sforza¹.

¹Functional Anatomy Research Center (FARC), Laboratorio di Anatomia Funzionale dell'Apparato Stomatognatico, Dipartimento di Scienze Biomediche per la Salute, Facoltà di Medicina e Chirurgia, Università degli Studi di Milano, Milano, Italy.

²SST Studio Associato Sidoti & Tartaglia, Segrate (MI), Italy

MS #CLOI-S-13-01155 submitted to Clinical Oral Investigations on 30 November 2013 – first revision 02 March 2014
– second revision 07 June 2014

Running title: Clinical performance of zirconia crowns

Number of tables: 5

Number of figures: 1

Corresponding author:

Prof. Chiarella Sforza

Dipartimento di Scienze Biomediche per la Salute

via Mangiagalli 31

I-20133 MILANO – ITALY

TEL. +39 – 02 503 15407

FAX +39 – 02 503 15387

E-mail address: chiarella.sforza@unimi.it

ABSTRACT

1 *Objectives.* Zirconia based prostheses are used for aesthetic crown and fixed restorations, but follow ups are still
2 limited. The authors evaluated the 7-year clinical results of 303 zirconia core restorations, performed in a general dental
3 private practice.
4

5
6 *Materials and Methods.* Clinical events (fracture and loss of retention, gingivitis, tenderness, excess cement, temporary
7 pain) were recorded in 303 zirconia core restorations positioned in 88 patients. Kaplan-Meier survival probability
8 estimates were computed for failures (needed the replacement or removal of the prosthesis) and complications (resolved
9 without replacing the prosthesis).
10

11
12 *Results.* One hundred and fifty single crowns (130 tooth-supported, 20 implant-supported) and 153 multiple units up to
13 6 elements (49 tooth-supported, 104 implant-supported) were followed up for 7 years in 88 patients (40 men, 48
14 women), aged 35-89 years (mean 57). During the follow-up period, there were no complications for 287 (95%) of the
15 restorations. Sixteen restorations/abutment teeth (5%) had some complication: extraction of abutment tooth (7; 2%);
16 caries (2; 1%), porcelain veneer fracture (3; 1%), loss of retention (4; 1%). Nine (3%) restorations were recorded as
17 failures. The overall 7-year survival probability estimate for failures was 0.966 (95% confidence limits, 0.932 and
18 0.983), for complications was 0.976 (95% confidence limits 0.947 and 0.989), with a cumulative survival rate of 94.7%
19

20
21 *Conclusions.* Within the analysed follow-up, zirconia core restorations appear a good clinical solution, with favourable
22 functional properties.
23

24
25 *Clinical Relevance.* All ceramic restorations can be successfully used for both single and multiple unit prostheses, either
26 teeth or and implants supported.
27

28
29
30 **Key words:** Zirconia; All-ceramic; Single crown; Fixed Dental Prostheses; Implants; Clinical performance
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

INTRODUCTION

Crystalline ceramics like alumina and zirconia are currently being increasingly used as core materials for fixed dental prostheses (FDPs) [1-7]. Zirconia had been used in dentistry since 1989 with various scopes; in particular, the first FDPs were reported in 1998 [8].

Zirconia performs well from the aesthetic, biological and functional points of view, meeting the demand of the patients and dentists, also in the presence of higher occlusal loads than those borne by the conventional ceramics of the past [5, 9-12]. These high-strength ceramic materials are manufactured using computer aided design/computer assisted manufacturing (CAD/ CAM), and are considered as an alternative to conventional metal- ceramic restorations [2, 3, 5, 6, 10, 12-17].

Zirconia is a crystalline dioxide of zirconium; its yttrium oxide partially stabilized form (3Y-TZP) has favorable mechanical properties (high flexural strength and fracture toughness, high hardness), can well tolerate cyclical pressure, and it possesses an excellent biocompatibility with a color very similar to dental color [1, 3, 5, 10-12]. To obtain esthetically superior results, the zirconia cores are covered by veneering porcelain; this last is directly exposed to chewing, clenching, and moisture; fatigue mechanisms and stress corrosion further weaken the veneer and finally it could result in cracks or chippings [18]. If zirconia cores are accurately customized, the ceramic fracture rates are not statistically different from the clinical performance of conventionally luted metal–ceramic [4].

In a previous clinical prospective study, the authors reported 3-year follow-up data for a group of 142 patients, who had both single crowns (202 tooth-supported single crowns, 36 implant-supported single crowns) and multiple-unit (up to 6 elements) crowns (81 tooth-supported multiple crowns, 144 implant-supported multiple crowns). The overall cumulative survival rate (CSR) was 98.2%, without differences between tooth- or implant- supported crowns, either single or multiple [6], and in compliance with, or even better than, literature reports [12, 17, 19, 20]. Overall, zirconia core crowns had favourable aesthetic and functional properties.

Other investigations reported follow up times up to 5 years, but almost always for reduced numbers of crowns [1-3, 5, 7, 12, 20-22]. Only Ortorp et al. [2] reported data on more than 140 crowns (but they only examined the clinical records not the patients), and Schley et al. [12] estimated the 5-year survival rate of nearly 300 zirconia crowns reviewed from literature. The longest follow-up seems to be that reported by Sax et al. [23], who examined 26 crowns after 10 years with a resulting 67% CSR.

Considering that the clinical performance of prosthetic reconstructions should be assessed at 5 years at least [2, 22, 24], further longitudinal analyses, with a longer follow-up and a sufficient number of prostheses in all parts of the mouth, are considered to be necessary.

Alongside with in vitro testing, clinical data are necessary to identify the frequency of failures (chipping, cracks) in veneered zirconia crowns, so that protocols to reduce their occurrence may be devised: using an anatomically designed substructure, an appropriate veneering technique, and an adapted cooling protocol [18].

The aim of the current clinical follow-up study was to evaluate the 7-year clinical results of a large number of zirconia core crowns, performed in a general dental private practice. Both single crowns and multiple units, supported by either teeth or implants, were followed up.

MATERIALS AND METHODS

Patient selection

1 On September 2012 all patients included in a previous study [6] were selected from dental hygiene clinical recall
2 appointments. The general inclusion criteria consisted of having received one or more zirconia crowns from the same
3 private practice between January 2005 and January 2006. Inclusion criteria were the needs for one or more, one to
4 three- six unit fixed dentures supported by either implants or teeth [6]. Tooth supported prostheses were used only on
5 root canal treated teeth and teeth with successful endodontic revision.

6 The teeth with different grades of irreversible pulpitis [25] were root-canal treated. The teeth with broken instruments,
7 root canal overfilling, incorrect working length, mechanical perforations in absence of periradicular lesions and
8 periodontal disease were nonsurgically endodontic revised. Root canal treatments were performed only to cure an
9 existing non healthy condition. All teeth received a prefabricated post [26].

10 Prior to prosthodontic treatment, all the patients were examined by a dental hygienist and were found to have good or
11 moderate oral hygiene with less than 25% marginal plaque [27], and no caries. They declared to had received less than
12 five new restorations during the preceding five-year period. When necessary, preliminary dental treatment was
13 performed to obtain the aforementioned inclusion criteria. Good general health without severe medical or psychological
14 conditions was generally self-reported by patients. All subjects provided informed consent for the clinical procedures, in
15 accordance with Helsinki declaration and Italian Law.

16 For tooth-supported prostheses, the bone level of the supporting teeth was at least half the root length and there were no
17 signs of active bone resorption, furcation involvement, mobility, or periapical pathology. Furthermore, the residual
18 coronal tooth structure was shown to have a tooth restorability index value equal to or less than 2, that is there was no
19 sufficient residual coronal dentine for restoration [8].

20 The patients were informed about the second step of the study, and agreed to be a part of the investigation. All subjects
21 had confirmed their already provided informed consent to the clinical procedures in conformity with current guidelines
22 for good clinical practice [28] and the current Italian law. From the original 138 patients analyzed in the 3-year follow-
23 up, only 88 patients were visited and continued their treatment. The 50 patients (36% of total) lost to follow-up had a
24 total of 142 crowns (32% of total crowns); the lost patients moved from the area (14 patients, 10% of total recalled),
25 deceased (11 patients, 8%), or did not answer to the recall (25 patients, 18%).

26 The study was therefore performed on the remaining 88 patients (41 men, 48 women), aged between 35 and 89 years
27 (mean age 59 years, SD 13; women, mean age 58 years, SD 13; men, mean age 60 years, SD 13; no age differences
28 between men and women, Student's t test, $p = 0.400$) with a total number of 303 crowns. All the patients were visited
29 by an independent operator that had not been involved in the original prosthetic procedures.

30 Survival rate was defined as surviving FDPs minus altered FDPs based on two (grades 2 and 3) of the three grades scale
31 of chipping fractures [30]. Surface chipping is graded 1 if the fractured surface is not extended into a functional area
32 and polishing is possible. Recontouring will result in an acceptable alteration of the anatomic form from the original
33 anatomy.

34 *Clinical procedures for zirconia crowns*

35 The clinical procedures were detailed in a previous investigation study [6]. In brief, all patients had indications for one
36 or more, one to three-six unit fixed dentures supported by either implants or teeth.

37 All the teeth had a tooth restorability index equal to or less than 2 [6], that is there was no sufficient residual coronal
38 dentine for restoration from operator judgment [8]. A core was built up with a composite material (LuxaCore, DMG
39 Hamburg Germany) if the occlusal space was more than 2 mm in centric occlusion.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

All teeth preparations were made in a standardized manner, with an occlusal reduction of 2 mm, axial reduction of 1.5 to 2 mm, and a 10-degree taper following the scalloping of the free gingival margins [24]. The residual abutment need to be at least 4 mm high from the buccal and lingual gingival margins to the occlusal surface. All multiple three to six units had a total gap equal or not exceeding crown-root surface area of abutment teeth in comparison of the teeth to be restored, with a minimum of 3 mm of occlusogingival height from the col of the interproximal papilla to the marginal ridge of the prospective abutments adjacent to the space to be restored. For both implants (pick-up technique) and teeth polyether (Impregum/Permadyne, 3M ESPE AG, Seefeld, Germany) was used for the impressions in a customized tray (Apex trays, Megadenta Dentalprodukte Radeberg, Germany). Individualized, provisional resin crowns (Takilon BB, Salmoiraghi srl, Melegnano, Lodi, Italia) were cemented using a temporary zinc oxide-eugenol (ZOE) cement (Temp Bond, Kerr Italia, Scafati, Salerno, Italia). A plaster model (Esthetic-base gold, Dentona AG, Dormund, Germany) was obtained and used to create an anatomical contour wax-up. The wax contour was then impressed on the plaster model. The plaster model, the silicone mask, and then both components together were scanned with a laser scanner (Everest Scan pro, Kavo, Biberach, Germany). The zirconia core was designed with respect to the ceramic support. At the occurrence the STL files were transformed in JGESS files with a reverse engineering technique (Geomagic, Research Triangle Park, NC, USA) and accurately quoted and modified with a CAD system (Rhinoceros, Seattle, WA, USA) For implant-supported prostheses, all implants (Titanmed, Milde Implants, Bergamo, Italy) showed good osseointegration at both clinical, instrumental (resonance frequency analysis) and radiographic tests [30]. Implant abutments (titanium) were prepared with the same principles outlined for teeth on the dental cast. For crown thickness, the core was covered by a uniform thickness of veneering ceramic, with a maximum of 2 mm of unsupported porcelain. Zirconia core was designed in respect of the ceramic support. The connectors for multiple-unit zirconia-crowns were designed with a 10 mm² area at least. Area measures were directly obtained from the software used for the CAD technique. The zirconia core was milled in the pre-sintered state (Zirite, Keramo, Tavernerio, Como, Italia) using Computer Aided Manufacturing (CAM), and subsequently sintered in accord with the manufacturer (TFR, Udine, Italia). Feldspathic porcelain (CZR Noritake Kizai Co. Ltd, Nagoya, Japan) was fused on the core with zirconium oxide margins by one master ceramist in accordance with a slow cooling protocol [31, 32]. Proximal contact points and occlusal contacts were adjusted as necessary and tested in maximum intercuspation with no interferences in lateral excursions by using 8-mm-wide, 8-mm-thick shim stocks (Hanel, Roeko, D-89122 Langenau, Germany). Pearl surface (Noritake Kizai Co. Ltd, Nagoya, Japan) paste was utilized for final crowns polishing and luster prior of insertion. The abutment teeth or implants were cleaned before cementation. For final cementation, a glass-ionomer cement was used (Ketac, 3M ESPE AG, Seefeld, Germany). Antagonist elements had to be present on teeth, fixed prostheses or implants, excluding removable prostheses. All patients were submitted to functional analysis of their masticatory muscles just before and after the cementation of the final prostheses according to a previously standardized protocol [33]. All patients had a good neuromuscular equilibrium [34, 35].

Data collection and analysis

At the 7-year follow up visit, for each patient, the same variables included in the 3-year follow up study were obtained: gender, age at crown delivery, number of cemented crowns, type of crowns (i.e., single or multiple units prostheses), tooth position, type of support (i.e., dental root or implant). For the patients assessed at the 7-year follow-up visit, the mean observation time was 83.89 months (SD 0.71), ranging from 78 to 84 months.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

In accordance with Ortorp et al. [2], clinical events were recorded as complications or as failures. Complications were technical (loss of retention, crown fractures) and biological (secondary caries, periodontal problems, tenderness, excess cement, temporary pain), and were resolved without replacing the zirconia prosthesis. Failures needed the replacement or removal of the prosthesis, and were due to fracture and loss of retention of the prosthesis, extraction of the abutment tooth or loss of osteointegration of the implant; secondary caries or persistent pain.

The distributions of crowns either into single or multiple units, or according to their kind of support and position in the mouth, in the original group of patients (138 patients at 3 years after cementation [6]), in the lost to follow up patients (50 patients), and in the remaining (currently analysed) 88 patients were tested by Chi-Square tests.

Kaplan-Meier estimates of overall survival time and complications-free rate time were calculated for the analyzed group of zirconia crowns [7, 22]. The method measured the fraction of crowns survived for a certain amount of time after final cementation, considering also the effect of lost to follow up (or censored) crowns. In survival analysis, patients were censored if they had not experienced the end-point of interest at the end of the follow up.

To take into account multiple data for the same patient and considering that in some groups (failures in men, complications in multiple crowns, etc., see below) there were no events, Cox regression model with Robust estimate cluster variance (patients are the cluster variable) was calculated for each independent variable (gender, type of support, position and number of crowns, age). Clustering effects within patient (correlation within multiple records on the same patient) were adjusted using robust standard errors.

Hazard ratios (HR) and respective 95% confidence limits (CI) were calculated. Model assumption of proportional hazards was assessed through graphical inspection and statistical tests. Considering collinearity between gender, kind of support and numbers of crowns (all events are only in one class of these variables) no multivariable model was fitted.

To allow an easier comparison with previous investigations, the cumulative survival rate (CSR) was also calculated according to the life table technique [2, 6].

Statistical significance was set at 5% (p value <0.05) for all analyses listed before.

RESULTS

From the original 142 patients who had received zirconia crowns between January 2005 and January 2006 in the same private dental practice, four patients (2.82%) with a total of 18 crowns (4% of the total original crowns) had already dropped from the study at the 3-year follow up, leaving a group of 138 patients (Table 1) [6]. Other 50 patients were lost for the current 7-year follow up examination (Table 2). The study was therefore performed on 88 patients (64% of the original group).

These patients had 150 single crowns (130 tooth-supported, 20 implant-supported) and 153 multiple units up to 6 elements (49 tooth-supported, 104 implant-supported). Most of the crowns (73% of the total number of crowns examined at the 7-year follow up) were on posterior teeth (premolar-molar area), and 41% of them were implant-supported (Table 3). There were no significant differences in the distribution of crowns into single or multiple units among the original 3-year patients, the dropped out patients and the 7-year analyzed patients (Chi-Square test, p = 0.754). Additionally, no differences in the distribution of prostheses according to their kind of support and position in the mouth were found among the three groups (Chi-Square test, p=0.999)

There were no complications recorded for most of the crowns during the follow-up period. Out of the 303 crowns that were followed up for 7 years, 287 (94.7%) experienced no complications. Only 16 crowns/ abutment teeth (5.3%) experienced some type of complications or failures (Table 4). The main recorded failures were extraction of abutment tooth (2.3% of total crowns) and secondary caries (0.7%). Among complications there were minor porcelain veneer

fractures that were easily polished (1%), loss of retention of the crowns that could be re-cemented (1.3%). All failures and complications were observed in separate patients, no patient had more than one event, independently from the number or kind of prostheses present in the mouth.

Seven years Kaplan-Meier survival probability estimate of failures for the total group of prostheses was 0.966 (95% confidence limits 0.932 and 0.983, Figure 1). Similar values were obtained for the 7-year CSR (94.7%). All failures were observed in women (incidence, 0.07%), in tooth-supported prostheses (incidence, 0.06%) and in single crowns (0.07%), with a significant difference between genders ($p < 0.001$), kinds of support ($p < 0.001$) and numbers of crowns ($p < 0.001$). Position in the mouth did not influence failures ($p = 0.316$): one failure was found in anterior prostheses (0.01%), and eight failures were found in posterior prostheses (0.04%). Age was inversely related to failure risk (Cox univariate regression, HR = 0.94, 95% CI 0.9-1.0, $p = 0.076$), but the relationship was at the limit of statistical significance.

In the assessment of complications for the total group of prostheses, seven years Kaplan-Meier survival probability estimate was 0.976 (95% confidence limits 0.947 and 0.989, Figure 1). Five complications were reported in women (incidence, 0.04%), and two in men (0.02%), without statistically significant differences ($p = 0.355$). Neither kind of support (six complications in tooth-supported prostheses, one in implant-supported prostheses, $p = 0.217$), nor position in the mouth (four complications in anterior crowns, three in posterior ones, $p = 0.206$) influenced complications. Seven complications were reported in single crowns (0.06%), while multiple units prostheses had no complications ($p < 0.001$). No significant effects of age were found for complications (Cox univariate regression, HR = 0.99, 95% CI 0.9-1.1, $p = 0.677$).

DISCUSSION

In the current clinical longitudinal study, the 7-year follow-up results of more than 300 single or multiple units zirconia core crowns, supported by either root canal treated teeth or implants were evaluated. The authors focused their attention only in terms of binary success and failure categories of the zirconia prostheses. In particular, possible subclinical endodontic problems that could be detected from an intraoral radiograph were not considered in detail. Indeed, the crossover among studies on zirconia based fixed dental prostheses is limited [36], and general considerations of survival rates, with and without minor and major interventions, may permit less biased comparisons among dental specialties [37].

The number of prostheses appears to be one of the largest in literature for follow-up examinations of 5 or more years, being 4-10 times larger than that found in most reports (Table 5). The number of tooth-supported prostheses (179) was comparable to that reviewed by Schley et al. [12] in their literature meta-analysis, and by Ortorp et al. [2] in their retrospective study. The statistical unit of the current investigation was the prosthesis and not the patient. Indeed, when considering more than one restoration per patient, the events are not independent because some patients may be more likely to have failures or complications than others. The effect was adjusted using robust standard errors. Similar procedures (more than 1 unit per patient) were reported by most previous investigations [2-5, 7, 9, 14-17, 20, 21, 23, 41, 44]. Only a limited number of reports used only one restoration per patient [22, 43].

The dropout rate of the crowns in the current study was 32% within 7 years, well within literature reports stating dropout ranges between 0-66% [38]. The dropout percentage is well comparable to 5-years literature reports where more than 100 crowns were followed up, that ranged from 24 to 46% [2, 7, 21, 22], and in good accord with the only 10-years study that stated a 54% dropout rate [23].

1
2
3
4
5
6
7
8
9
Indeed, dropped out patients may be unsatisfied with the treatment, thus provoking a positive selection bias of the analyzed sample, with a resulting positive overestimation of the survival and success rates. However, in half of the cases the reasons for not attending the follow up visit were unrelated to the patient satisfaction (moving out of the area, death). Additionally, no significant differences were found in the distribution of prostheses according to their support and location in the dental arch among the original group, the dropped out and the analyzed prostheses. In accord with previous investigations [4], the authors believe that there is no increased risk for a selection bias. Indeed, the inclusion of patients from a private practice, where the patient- dentist relationship is based also on emphatic considerations, allows considering all factors entering into the general “satisfaction”.

10
11
12
13
14
15
16
17
18
19
20
According to the classification reported by Anusavice [29], the current results may be considered of excellent performance, with a survival of 95–100% of all the prostheses for at least five years and a success rate of 90–95%. When considering literature reports, the current data are among those with the best survival rates, estimated either with Kaplan-Meier method or with the CSR (Table 5): better percentages were reported only by Pelaez et al. [16], Tartaglia et al. [6], Wolfart et al. [17] and Sorrentino et al. [5] but for shorter follow-up times (3 to 5 years). Kaplan-Meier method allowed taking into consideration also those crowns that were lost to follow-up (censored observations), thus providing a better estimate of zirconia prostheses survival [22].

21
22
23
24
25
26
27
28
29
30
31
Al-Amleh et al. [1] reviewed the literature reporting the clinical performance of approximately 600 zirconia crowns, but only 52 were followed up for 5 years, with survival rates between 74 and 100%; fractures and secondary caries were the most common causes of failure. In particular, chipping of the veneering porcelain seems to be the major complication, with percentages ranging from 6 to 25% for 3 to 5-year follow up examinations [3, 4, 8, 17, 20, 22, 39]. Papaspyridakos and Lal [14] followed-up for 2-4 years 16 dental arches restored with implant-supported zirconia prostheses (12-14 multiple units), and reported that porcelain fracture was the most frequent technical complication, with a 31% chipping rate.

32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
Overall, when compared to literature, a lower rate of veneer chipping and fractures was found, as only three crowns out of 303 (less than 1%) had some minor chipping that did not require a new prosthesis [5, 23]. Indeed, not only the incidence of veneer chipping has been reported to be related to the duration of clinical service [23], but also an anatomical design of the zirconium dioxide frameworks that support the veneering porcelain was found to be related to a reduced incidence of porcelain chipping [3]. Indeed, at 7 years observation time failures and complications were found only in single unit prostheses, and not in multiple units ones. This result is in partial contrast with the data presented in the previous study at the 3-year follow up [6], where fractures were observed only in prostheses with more than 3 units, and were located in the interdental connectors or in the zirconia core next to the connectors, in accordance with literature findings [10, 20]. The moment of crown failure may be explained by two different factors: early failures may be ascribed to fabrication problems, whereas late failures may be produced by wear or deterioration of the material [18].

49
50
51
52
53
54
55
Another factor leading to porcelain chipping is an inappropriate thickness of the zirconia veneer [4, 7, 15, 18, 22]. Pelaez et al. [15] also reported that occlusal contact may be a factor for chipping. In the prostheses included in the study, porcelain was fused on the zirconium core using a slow cooling protocol, that has been reported to be one of the factors for a successful crown performance [7, 31, 32]. Poor results may be also due to some particular kind of crystalline ceramic [22].

56
57
58
59
60
61
62
63
64
65
Apart from technical aspects, porcelain chipping can be also related to the force developed by every single patient over the prostheses, a still uncontrolled variable during oral rehabilitation procedures [7, 40]. Indeed, some relationship between age and crown failures were found: younger patients were at larger risk than older patients. This may be

1 tentatively explained by the best muscular performances that younger patients could perform, and that could damage the
2 prostheses. In contrast, all failures were observed in women, that should possess less forceful masticatory muscles than
3 men. Unfortunately, the effect of gender on zirconia crown performance does not seem to have been analysed in
4 literature, and even recent investigations and reviews did not report information on this aspect [7, 14, 22, 36].

5 A functional analysis of the masticatory muscles has already been suggested as a tool to obtain indicative values for the
6 occlusal loads to be resisted by the prosthetic reconstructions [40]. As discussed in the previous investigations [6], in all
7 the analysed patients occlusal reduction was attentively checked during preparation, and only minor or no occlusal
8 adjustments were necessary. This may depend by the functional control of all prostheses: the masticatory muscles of all
9 patients were examined from a functional point of view just before and just after the cementation of the final prostheses
10 [6]. All patients had a good equilibrium (symmetry, torsion, anterior-posterior balance) among their masticatory
11 muscles, and their new occlusal conditions were properly incorporated into their stomatognathic system [34, 35]. In
12 contrast, Passia et al. [22] reported that the thickness of their crowns may have been inappropriately reduced during
13 final occlusal control (before cementation). Moreover, the relatively low incidence of loss of retention in spite of the
14 conventional cementation used could be tentatively explained by morphological considerations. A careful crown
15 design, with a fine geometrical match between crown and abutment is a prerequisite. To obtain this goal, the abutment
16 were 4 mm high at least as above mentioned [42].

17 Veneer fracture of porcelain (1% of crowns) and loss of retention (1%) were the only other complication reported in the
18 7-year follow-up, while failures were due to secondary caries (0.7%) and need of extraction of the abutment tooth (2%).
19 Indeed, tooth-supported prostheses had a significantly higher failure rate than implant-supported ones: previous root-
20 canal treatment may be a factor explaining this finding.

21 The low incidence of secondary caries seen in the patients included in the study, seems in contrast with some previous
22 literature studies [12, 20, 22]. It has to be mentioned that in some clinical studies the incidence of secondary caries may
23 be over-evaluated, because the presence of recurrent caries can be made from the clinical point of view only, and
24 marginal discoloration could be mistaken for a sign of caries [6]. Unfortunately, only histological assessment can
25 confirm the clinical diagnosis.

26 One of the limitations of the current investigation is the absence of a control group, as done in other clinical trials [4, 7,
27 9, 15, 22, 43]. However, the current study was made in one private practice, where zirconia is the only material used for
28 single and multiple units' crowns [6]. Additionally, all the crowns were fabricated at one laboratory and all teeth/
29 implants were treated with the same standardized protocol by the same clinical staff. Similar considerations were made
30 by Ortorp et al. [2]. An advantage of the current study relative to other investigation is the direct assessment of the
31 patients during a dental control visit, while Ortorp et al. [2], in their 5-year follow-up study, used information recorded
32 in the clinical notes.

33 The use of all ceramic dental prostheses is becoming widespread, well replacing the conventional metal-ceramic FDPs
34 in the entire dental arch. Christensen and Ploeger [9], Pelaez et al. [15] and Vigolo and Mutinelli [43] in randomized
35 controlled clinical studies found no significant differences in CSR between conventional metal prostheses and zirconia
36 crowns; similar conclusions were reported by Rinke et al. [4] after a prospective clinical study. Different results were
37 reported by Passia et al. [22], who found that their shrinkage-free zirconia crowns had a 3.13-fold higher probability of
38 failure than the conventional gold crowns. Overall, a recent meta-analysis found that the estimated 5-yr survival rate
39 and the estimated failure rates of zirconia and metal-ceramic FDPs were comparable [12]. These results are not yet
40 confirmed for the long-span FDPs in the molar region that are at greater risk of failure than the FDPs in the anterior
41

region [22, 32], even if no differences in the estimated survival rates of anterior and posterior prostheses were found (Figure 1).

In conclusion, even after 7 years for service, zirconia core crowns appear a good clinical solution for both single and multiple unit prostheses, with favourable functional properties.

The present clinical data are in good accord with literature findings, and, to the authors' knowledge, represent the first 7-year follow up study performed in a private dental practice. The number of analysed patients and crowns, and the variety of prostheses (single and multiple units) and supports (teeth and implants), may offer a good help to the dentist for everyday clinical decisions.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Al-Amleh B, Lyons K, Swain M (2010) Clinical trials in zirconia: a systematic review. *J Oral Rehabil* 37:641-652
2. Ortorp A, Kihl ML, Carlsson GE (2012) A 5-year retrospective study of survival of zirconia single crowns fitted in a private clinical setting. *J Dent* 40:527-530
3. Raigrodski AJ, Yu A, Chiche GJ, Hochstedler JL, Mancl LA, Mohamed SE (2012) Clinical efficacy of veneered zirconium dioxide-based posterior partial fixed dental prostheses: five-year results. *J Prosthet Dent* 108:214-222
4. Rinke S, Schäfer S, Lange K, Gersdorff N, Roediger M (2013) Practice-based clinical evaluation of metal-ceramic and zirconia molar crowns: 3-year results. *J Oral Rehabil* 40:228-237
5. Sorrentino R, De Simone G, Tetè S, Russo S, Zarone F (2012) Five-year prospective clinical study of posterior three-unit zirconia-based fixed dental prostheses. *Clin Oral Investig* 16:977-985
6. Tartaglia GM, Sidoti E, Sforza C (2011) A 3-year follow-up study of all-ceramic single and multiple crowns performed in a private practice: a prospective case series. *Clinics (Sao Paulo)* 66:2063-2070
7. Burke FJ, Crispa RJ, Cowanb AJ, Lambc J, Thompsond O, Tulloche N (2013) Five-year clinical evaluation of zirconia-based bridges in patients in UK general dental practices. *J Dent* 41:992-999
8. Ozkurt Z, Kazazoğlu E (2010) Clinical success of zirconia in dental applications. *J Prosthodont* 19:64-68
9. Christensen RP, Ploeger BJ (2010) A clinical comparison of zirconia, metal and alumina fixed-prosthesis frameworks veneered with layered or pressed ceramic: a three-year report. *J Am Dent Assoc* 141:1317-1329
10. Denry I, Kelly JR (2008) State of the art of zirconia for dental applications. *Dent Mater* 24:299-307
11. Manicone P, Iommetti P, Raffaelli L (2007) An overview of zirconia ceramics: Basic properties and clinical applications. *J Dent* 35:819-826
12. Schley JS, Heussen N, Reich S, Fischer J, Haselhuhn K, Wolfart S (2010) Survival probability of zirconia-based fixed dental prostheses up to 5 yr: a systematic review of the literature. *Eur J Oral Sci* 118:443-450
13. Çehreli MC, Kökat AM, Akça K (2009) CAD/CAM Zirconia vs. slip-cast glass-infiltrated Alumina/Zirconia all-ceramic crowns: 2-year results of a randomized controlled clinical trial. *J Appl Oral Sci* 17:49-55
14. Papaspyridakos P, Lal K (2013) Computer-assisted design/computer-assisted manufacturing zirconia implant fixed complete prostheses: clinical results and technical complications up to 4 years of function. *Clin Oral Implants Res* 24:659-665
15. Peláez J, Cogolludo PG, Serrano B, Serrano JF, Suárez MJ (2012) A four-year prospective clinical evaluation of zirconia and metal-ceramic posterior fixed dental prostheses. *Int J Prosthodont* 25:451-458

16. Peláez J, Cogolludo PG, Serrano B, Lozano JF, Suárez MJ (2012) A prospective evaluation of zirconia posterior fixed dental prostheses: three-year clinical results. *J Prosthet Dent* 107:373-379
17. Wolfart S, Harder S, Eschbach S, Lehmann F, Kern M (2009) Four-year clinical results of fixed dental prostheses with zirconia substructures (Cercon): end abutments vs. cantilever design. *Eur J Oral Sci* 117:741-749
18. Preis V, Letsch C, Handel G, Behr M, Schneider-Feyrer S, Rosentritt M (2013) Influence of substructure design, veneer application technique, and firing regime on the in vitro performance of molar zirconia crowns. *Dent Mater* 29:113–121
19. Encke BS, Heydecke G, Wolkewitz M, Strub JR (2009) Results of a prospective randomized controlled trial of posterior ZrSiO(4)-ceramic crowns. *J Oral Rehabil* 36:226-235
20. Sailer I, Fehér A, Filser F, Gauckler LJ, Lüthy H, Hämmerle CH (2007) Five-year clinical results of zirconia frameworks for posterior fixed partial dentures. *Int J Prosthodont* 20:383-388
21. Kokubo Y, Sakurai S, Tsumita M, Ogawa T, Fukushima S (2009) Clinical evaluation of Procera AllCeram crowns in Japanese patients: results after 5 years. *J Oral Rehabil* 36:786–791
22. Passia N, Stampf S, Strub JR (2013) Five-year results of a prospective randomised controlled clinical trial of posterior computer-aided design–computer-aided manufacturing ZrSiO₄-ceramic crowns. *J Oral Rehabil* 40:609-617
23. Sax C, Hämmerle CH, Sailer I (2011) 10-year clinical outcomes of fixed dental prostheses with zirconia frameworks. *Int J Comput Dent* 14:183-202
24. Raigrodski AJ, Chiche GJ, Potiket N, Hochstedler JL, Mohamed SE, Billiot S, Mercante DE (2006) The efficacy of posterior three-unit zirconium-oxide-based ceramic fixed partial dental prostheses: a prospective clinical pilot study. *J Prosthet Dent* 96:237-244
25. Sigurdsson A (2003) Pulpal diagnosis. *Endodontic Topics* 5:12–25
26. Bandlish RB, McDonald AV, Setchell DJ (2006) Assessment of the amount of remaining coronal dentine in root-treated teeth. *J Dent* 34:699–708
27. O'Leary TJ, Drake RB, Naylor JE (1972) The plaque control record. *J Periodontol* 43:38.
28. ICH E6 (1996) Good Clinical Practice: Consolidated Guidance. U.S. Food and Drug Administration <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm219488.htm>
29. Anusavice KJ (2012) Standardizing failure, success, and survival decisions in clinical studies of ceramic and metal–ceramic fixed dental prostheses. *Dent Mater* 28:102-111
30. Sennerby L, Meredith N (2000) Implant stability measurements using resonance frequency analysis: biological and biomechanical aspects and clinical implications. *Periodontology* 47:51–66.
31. Guazzato M, Walton TR, Franklin W, Davis G, Bohl C, Klineberg I (2010) Influence of thickness and cooling rate on development of spontaneous cracks in porcelain/zirconia structures. *Aust Dent J* 55:306-310.
32. Schimtter M, Mussotter K, Rammelsberg P, Gabbert O, Ohlmann B (2012) Clinical performance of long-span zirconia frameworks for fixed dental prostheses: 5-year results. *J Oral Rehabil* 39:552–557
33. Ferrario VF, Sforza C, Colombo A, Ciusa V (2000) An electromyographic investigation of masticatory muscles symmetry in normo-occlusion subjects. *J Oral Rehabil* 27:33-40
34. Ferrario VF, Tartaglia GM, Galletta A, Grassi GP, Sforza C (2006) The influence of occlusion on jaw and neck muscle activity: a surface EMG study in healthy young adults. *J Oral Rehabil* 33:341-348

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

35. Tartaglia GM, Testori T, Pallavera A, Marelli B, Sforza C (2008) Electromyographic analysis of masticatory and neck muscles in subjects with natural dentition, teeth-supported and implant-supported prostheses. *Clin Oral Implants Res* 19:1081-1088

36. Raigrodski AJ, Matthew B, Hillstead MB, Meng GK, DDS, Chung KH (2012) Survival and complications of zirconia based fixed dental prostheses: A systematic review. *J Prosthet Dent* 107:170-177

37. Torabinejad M, Anderson P, Bader J, Brown LJ, Chen LH, Goodacre CJ, Kattadiyil MT, Kutsenko D, Lozada J, Patel R, Petersen F, Puterman I, White SN (2007) Outcomes of root canal treatment and restoration, implant-supported single crowns, fixed partial dentures, and extraction without replacement: a systematic review. *J Prosthet Dent* 98:285-311

38. Pjetursson BE, Sailer I, Zwahlen M, Hämmerle CHF (2007) A systematic review of the survival and complication rates of all-ceramic and metal–ceramic reconstructions after an observation period of at least 3 years. Part I: single crowns. *Clin Oral Implants Res* 18:73–85

39. Kern T, Tinschert J, Schley JS, Wolfart S (2012) Five-year clinical evaluation of all-ceramic posterior FDPs made of In-Ceram Zirconia. *Int J Prosthodont* 25:622-624

40. Ferrario VF, Sforza C, Zanotti G, Tartaglia GM (2004) Maximal bite forces in healthy young adults as predicted by surface electromyography. *J Dent* 32:451-457

41. Ernst CP, Cohnen U, Stender U, Willershausen B (2005) In vitro retentive strength of zirconium oxide ceramic crowns using different luting agents. *J Prosthet Dent* 93:551-558

42. Güth J-F, Wallbach J, Beuer F, Edelhoff D (2013) Computer-aided evaluation of preparations for CAD/CAM-fabricated all-Ceramic crowns. *Clin Oral Investig* 17:1389-1395

43. Vigolo P, Mutinelli S (2012) Evaluation of zirconium-oxide-based ceramic single-unit posterior fixed dental prostheses (FDPs) generated with two CAD/CAM systems compared to porcelain-fused-to-metal single-unit posterior FDPs: a 5-year clinical prospective study. *J Prosthodont* 21:265-269

44. Beuer F, Edelhoff D, Gernet W, Sorensen JA (2009) Three-year clinical prospective evaluation of zirconia-based posterior fixed dental prostheses (FDPs). *Clin Oral Investig* 13:445-451

Figure legend

Fig. 1 Kaplan-Meier survival probability estimates for failures and complications in the total group of prostheses.

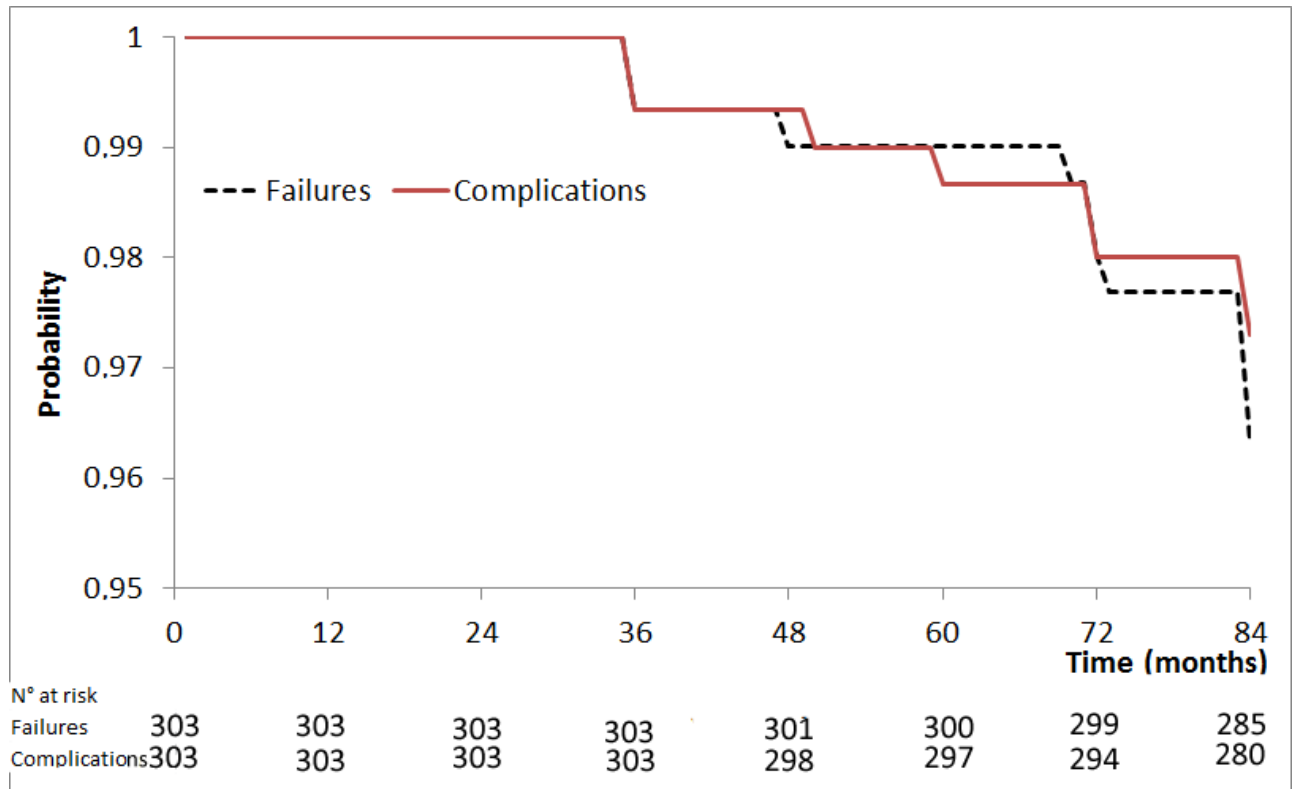


Table 1. Distribution of the 445 single and multiple-unit zirconia crowns on teeth and on implants by region.

	Single unit crowns		Multiple unit crowns						Total
			2-3 units		4-5 units		6 units		
	Teeth	Implants	Teeth	Implants	Teeth	Implants	Teeth	Implants	
Anterior	43	5	23	2	9	8	0	14	104
Posterior	159	21	15	64	20	50	12	0	341
Total	202	26	38	66	29	58	12	14	445

Table 2. Distribution of the 142 single and multiple-unit zirconia crowns on teeth and on implants by region lost to the 7-years follow up.

	Single unit crowns		Multiple unit crowns						Total
			2-3 units		4-5 units		6 units		
	Teeth	Implants	Teeth	Implants	Teeth	Implants	Teeth	Implants	
Anterior	17	0	5	0	0	0	0	0	22
Posterior	55	6	3	14	10	20	12	0	120
Total	72	6	8	14	10	20	12	0	142

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Table 3. Distribution of the single and multiple-unit zirconia crowns on teeth and on implants by region in the patients visited at the 7-year follow up.

		single unit								multiple units								total
		2-3 units				4-5 units				6 units								
		anterior		posterior		anterior		posterior		anterior		posterior		Anterior		posterior		
		maxilla	mandible	maxilla	mandible	maxilla	mandible	maxilla	mandible	maxilla	mandible	maxilla	mandible	maxilla	mandible	maxilla	mandible	
teeth	men	9	1	21	13	18	0	0	0	9	0	8	0	0	0	0	0	79
	women	14	2	40	30	0	0	11	1	0	0	0	2	0	0	0	0	100
implants	men	4	1	0	4	2	0	17	14	4	0	12	6	0	0	0	0	64
	women	0	0	3	8	0	0	6	13	4	0	8	4	14	0	0	0	60
Total no.		27	4	64	55	20	0	34	28	17	0	28	12	14	0	0	0	303

Table 4. All complications and reasons for failures of zirconia crowns.

	Anterior	Posterior	Total
Number of crowns	82	221	303
Complications			
Veneer fracture (polished)	1	2	3
Loss of retention (recemented)	3	1# (implant)	4
Other (gingivitis, temporary pain)	0	0	0
<i>Total no. of complications</i>	<i>4</i>	<i>3</i>	<i>7</i>
Failures			
Veneer fracture (new crown)	0	0	0
Loss of retention (new crown)	0	0	0
Extraction (teeth)	1	6	7
Caries	0	2	2
<i>Total no. of failures</i>	<i>1</i>	<i>8</i>	<i>9</i>

All complications and failures were on teeth-supported prostheses, except #

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Table 5. Zirconia prostheses in literature, from 3 to 10 years of follow-up.

Authors	Follow up years	No. of cemented crowns	No. of examined crowns	No. of complications	No. of failures	CSR (%)
Beuer et al., 2009 [44]	3	21	21	1	2	90.5%
Christensen and Ploeger, 2010 [9]	3	97	80		14	81-87%
Papaspyridakos and Lal, 2013 [14]	3	16 dental arches (12-14 multiple units)	16 dental arches (12-14 multiple units)	4	0	100%
Pelaez et al., 2012 [16]	3	20	20	2	1	95%
Rinke et al., 2013 [4]	3	55	52	4	2	95.2%
Tartaglia et al., 2011[6]	3	463	445	9	11	98.2%
Wolfart et al., 2009 [17]	4	58	55	14	5	92-96%
Pelaez et al., 2012 [15]	4	20	20	2	1	95%
Burke et al., 2013[7]	5	126	102	7	3	60-97%§
Kern et al., 2012 [39]	5	20	20	3	4	90%
Kokubo et al., 2009 [21]	5	101	75	3	9	90.2%
Ortorp et al., 2012 [2]	5	205	143	29	19	88.3%
Passia et al. 2013 [22]	5	123	77	--	44	73.2%§
Raigrodski et al., 2012 [3]	5	20	18	3	4	79-90%
Sailer et al., 2007 [20]	5	57	33	34	12	73.9%
Schley et al., 2010 [12]	5 (estimated)	330	297	96	19	94.3%
Sorrentino et al., 2012 [5]	5	48	48	3	0	100%
Vigolo and Mutinelli, 2012 [43]	5	40	39	7	3	79-85%
Sax et al., 2011 [23]	10	57	26	66	15	67%

§ Kaplan-Meier survival probability estimate

Figure 1
[Click here to download high resolution image](#)

