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CLINICAL ORAL IMPLANTS RESEARCH

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Clinical performance of two-piece zirconia implants in the posterior mandible and maxilla: a prospective cohort study over 2 years

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Key words: cohort study, implant survival, zirconia implants

Abstract

Objectives: To assess the clinical performance of two-piece zirconium implants over a period of up to 2 years.

Material & methods: A total of 52 patients with single-tooth gaps in the posterior mandible or maxilla received the same type of a two-piece zirconium implant system with customized heights of the transmucosal aspect. Fibreglass abutments were cemented and restored with fixed all-ceramic single crowns using a conventional loading protocol. The cumulative survival rate (primary outcome) was calculated according to the life table method, and Kaplan–Meier survival curves were used to estimate the survival function. Covariates (gender, implant position, implant diameter/length, oral surgeon) were tested using log-rank tests.

Results: A total of two target implants in 2 patients were lost after a functioning time of 8 months. The cumulative survival rate was 95.8%, and the mean survival time amounted to 32.9 months. Log-rank tests revealed a significant association for the covariate "oral surgeon" ($P = 0.047$). The Kaplan–Meier estimates of mechanical/technical and biological complications amounted to 2.1% and 37.5%, respectively. All implant sites revealed a marked increase of the vestibular mucosal level and gain of keratinized tissue at 24 months.

Conclusion: Within the limitations of a prospective cohort study, it was concluded that this two-piece zirconium implant/fibreglass abutment system can be successfully used in the clinical indication investigated.

With the development of high-strength zirconia, new ceramics were supposed to serve as an alternative material for dental implants. In particular, yttria-stabilized tetragonal zirconia polycrystal (Y-TZP) reveals a high flexural strength, a favourable hardness and fracture toughness as well as a suitable weibull modle, thus overcoming major drawbacks associated with previous aluminium oxide-based ceramics (Depprich et al. 2014). Moreover, Y-TZP ceramics are tooth-coloured, highly biocompatible (Hempel et al. 2010) and reported to be less prone to bacterial colonization (Rimondini et al. 2002), thus offering potential advantages over titanium.

Preclinical studies performed in various animal models provide some evidence that surface-modified zirconia implants were commonly associated with a bone–tissue response and removal torque similar to that noted for moderately rough titanium implants (Sennerby et al. 2005; Gahlert et al. 2010, 2012). However, these outcomes were depending on the surface treatments, thus suggesting that the microtopography seems to be a critical determinant for the osseointegration of zirconia implants (Manzano et al. 2014).

The currently available clinical data are limited but point to inferior survival (74–98% after 12–56 months) and success rates (79.6–91.6% after 6–12 months) when compared with those values noted for commonly used titanium implants (Depprich et al. 2014). It is important to emphasize that the latter systematic review was mainly based on studies reporting on one-piece implants, and the available literature on two-piece zirconia systems is still scarce (Nevins et al. 2011; Cionca et al. 2014; Payer et al. 2015). Recently, a two-piece zirconium implant system featuring customizable heights of the transmucosal aspect as well as cementable and modifiable glass fibre abutments was

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introduced to overcome some of the limitations associated with one-piece implants. A recent retrospective analysis revealed a cumulative survival rate of 96.5% after 3 years (Brüll et al. 2014). At the time being, however, observational studies on this specific zirconium implant system are lacking.

Therefore, the aim of the present prospective cohort study was to assess the clinical performance of customized two-piece zirconia implants restored with cemented fibreglass abutments and all-ceramic crowns in the posterior mandible and maxilla over an observation period of up to 2 years.

Material and methods

Study design and participants

This is a prospective cohort study aimed at investigating the survival rates (primary outcome) as well as biological, technical and mechanical complications (secondary outcomes) of a two-piece, screw-type and surface-modified (tetragonal pattern, high average surface roughness (Ra) of approx. 7 µm and a mean roughness depth (Rz) of approx. 40 µm) zirconium implant system (ZV3, Zircon Vision GmbH, Wolfratshausen, Germany). It was provided in two different diameters (4.5 mm or 5.0 mm) and three different lengths (9, 11 or 13 mm). The transmucosal part of the implant was slightly roughened and allowed for the fixation of a modifiable fibreglass abutment (ZV3) serving as retention for the prosthetic reconstruction. Each implant was individually manufactured (i.e. milled and sintered) in a way that the implant neck and subsequently the crown margin was located in an epimucosal position. This was based on preoperative clinical and radiographic analyses (i.e. reference body in contact with the mucosa) to estimate the vertical dimension of the available hard- and soft tissue compartments at the respective implant sites.

The study population consisted of 60 partially edentulous patients suffering from at least one missing tooth in the premolar/molar regions of either the upper or lower jaw and were in need of a fixed dental prosthesis (Table 1). If the patient was in need of more than one implant, the most anterior position was defined as target site. Each patient was given a detailed description of the procedure and was required to sign an informed consent before participation. The study was in accordance with the Helsinki Declaration of 1975, as revised in 2013, and the study protocol was approved by the ethics committee of the Heinrich Heine University, Düsseldorf, Germany. Treatments have been provided between November 2011 and April 2012.

Table 1. **Patient demographics and implant site characteristics**

Patient number (*n*)	48
Female	31
Male	17
Age (years)	47.6 ± 13.4
Observation period (months)	25.5 ± 5.8
Patients with multiple implant sites	15
Patients with 1/2/3 implants	33/10/5
Patients treated by surgeon 1/2/3	7/29/12
Target implant sites	48
Location Upper Jaw	13
Location Lower Jaw	35
Implant diameter (4.5/5.0 mm)	17/31
Implant length (9/11/13 mm)	2/45/1
Target implant sites with augmentation	19
Simultaneous grafting of a dehiscence-type defect	12
Internal sinus floor elevation	6
External sinus floor elevation	1

Inclusion criteria

For patient selection, the following inclusion criteria were defined: (1) age ≥18 and ≤80 years, (2) tooth extraction at least 6 weeks prior to implant placement, (3) no need of more than four implants, (4) full mouth bleeding on probing (FMBOP) and full mouth plaque score (FMPS) ≤ 25%, (5) no systemic diseases which could influence the outcome of the therapy (e.g. diabetes (HbA1c < 7), osteoporosis), (6) no intake of medications which may have an effect on bone turnover and mucosal healing (i.e. steroids, antiresorptive therapy), (7) no pregnancy or breastfeeding women, (8) no physical or mental handicaps that would interfere with the ability to perform adequate oral hygiene, (9) non-smoker or light smoking habits (<10 cigarettes per day), (10) treated chronic periodontitis and proper periodontal maintenance care, (11) no history of mucosal diseases or oral lesions, (12) no history of bruxism or clenching habits, (13) no history of adverse reactions to the materials used in this study, and (14) no general contraindications for surgical interventions.

Surgical procedure

Under local anaesthesia, midcrestal and bilateral vestibular releasing incisions were made and mucoperiosteal flaps elevated to expose the respective sites for implant insertion. Implant site preparation was performed under copious irrigation with sterile 0.9% physiological saline and according to the surgical guidelines provided by the manufacturer. Each implant had to be inserted with good primary stability (i.e. lack of clinical implant mobility) and in a way so that the borderline between the transmucosal and intrabony part at best coincided with the lingual bone crest (Fig. 1a). The respective diameter and length of the implants were chosen according to the individual clinical and radiological situation. Simultaneous grafting of buccal dehiscence-

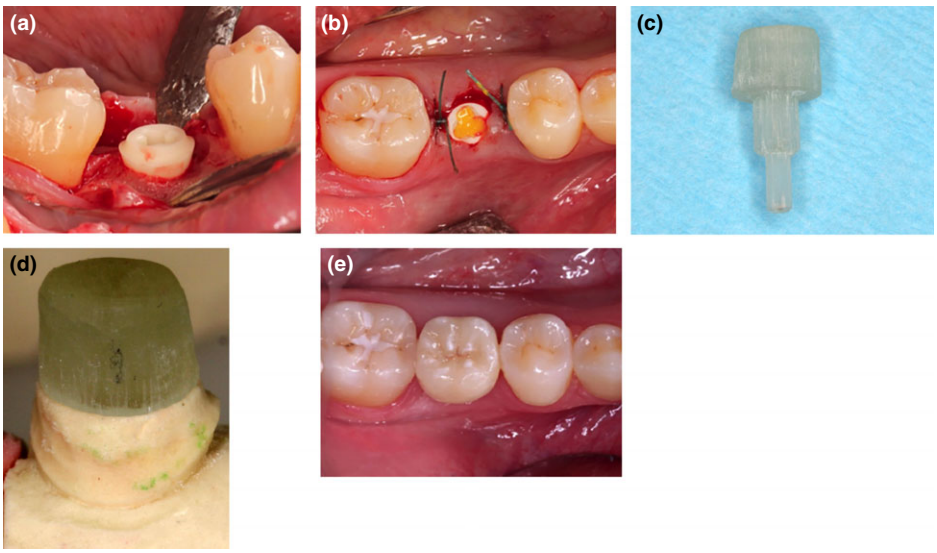

Fig. 1. Surgical procedures at baseline. (a) The posterior mandible or maxilla was selected as experimental site for implant placement in all patients. Situation after placement of the two-piece zirconium implant. (b) All sites were left to heal in a transmucosal position. (c) Cementable glass fibre abutment. (d) The abutments allowed for an individual crown preparation. (e) Situation after fixation of the fibreglass abutment and cementation of an all-ceramic single crown (Baseline).

type defects (Geistlich BioOss®, Geistlich Biomaterials AG, Wolhusen, Switzerland + Geistlich BioGide®, Geistlich Biomaterials AG) and internal sinus floor elevations were accomplished when necessary. External sinus floor elevation was associated with a staged implant placement at 4–6 months after grafting (BioOss®, BioGide®). All implants were left to heal in a transmucosal position without providing any temporization (Fig. 1b). All procedures were accomplished by three experienced and previously calibrated oral surgeons.

Prosthodontic procedure

A conventional implant loading was accomplished after a healing period of about 12 weeks in the maxilla and 10 weeks in the mandible. In particular, the glass fibre abutments allowed for a conventional chamfer preparation (Fig. 1c and d) and were fixed using a dual-cure resin cement and a self-adhesive primer (Panavia F2.0, Kuraray Europe GmbH, Hattersheim am Main, Germany). The abutment was part of the implant and certified as such. All implant system components were delivered sterile sealed in peel pouches and were opened immediately before application. Finally, conventional impressions (monophase polyether material, Impregum Soft, 3M ESPE, Neuss, Germany) were taken and all-ceramic single crowns (IPS monolithic e.-max crowns, Ivoclar Vivadent, Ellwangen, Germany) were fixed using the same resin cement, as recommended by the manufacturer. After cementation, the implant–abutment connection was completely covered (Fig. 1d). Due to the epimucosal position of the crown margins, cement remnants could be easily removed. Intraoral radiographs were taken to ensure the correct position of the respective components and detect residual cement.

Postoperative care

Postoperative maintenance care included a supramucosal-/gingival professional implant/tooth cleaning, local pocket irrigation using CHX and reinforcement of oral hygiene. Maintenance care was provided according to individual needs at 3, 6, 12, 18 and 24 months after therapy.

Clinical measurements

The following clinical parameters were assessed immediately after the cementation of the crown (baseline), and after 6, 12 and 24 months using a periodontal probe (PCP 12, Hu-Friedy, Tuttlingen – Moehringen, Germany): (1) plaque index (PI) (Löe 1967), (2) bleeding on probing (BOP), (3) probing depth (PD) – measured from the mucosal margin to the probeable pocket, and (4) mucosal recession (MR) – measured from the crown margin to the mucosal margin. All measurements were performed at six aspects per implant: mesiobuccal (mb), midbuccal (b), distobuccal (db), mesiooral (mo), midoral (o) and distooral (do) by two previously calibrated investigators. Implant mobility (i.e. loss of osseointegration) was measured by manual palpation. Due to the author's interpretation of the 84/466/EURATOM directive, radiographs for the longitudinal assessment of interproximal bone level changes were not justified. Subsequent to the surgical intervention and according to clinical standard procedures, additional radiographs were just taken after cementation of the crown, or when clinical signs suggested the presence of biological (i.e. BOP and/or suppuration)- or mechanical/technical complications.

Matrix metalloproteinase-8

At 6, 12 and 24 months and after a gentle supramucosal cleaning, peri-implant sulcus fluid was collected at the deepest aspect of each target implant site by means of sterile paper points (i.e. each was left in place for 30 s). These samples were sent to a commercial provider of laboratory services (Bioscentia MVZ Berlin) and analysed for active matrix metalloproteinase-8 (aMMP-8) to immunologically assess peri-implant inflammation.

Survival and complications

Implants were considered as survivals if they were present at the final follow-up examination after 24 months. Mechanical complications were considered to be all events affecting the integrity (e.g. fractures) of the implant and the fibreglass abutment. Technical events were considered to be those affecting the cemented crown (refers to a recent definition proposed by Heitz-Mayfield et al. 2014). Biological complications considered the presence of peri-implantitis (i.e. BOP with or without pus and changes in the radiographic bone level compared to baseline – i.e. intraoral radiograph taken at the time of prosthesis installation) at the target implants (Lang et al. 2011). To account for radiographic measurement errors, a threshold of 1.0 mm (manually assessed from the implant neck to the crestal bone level at both interproximal aspects using a grid) was considered for the assessment of bone loss (Sanz et al. 2012).

Statistical analysis

A commercially available software program (IBM SPSS Statistics 22.0, IBM Deutschland GmbH, Ehningen, Germany) was used for the statistical analysis. The cumulative survival rate was calculated according to the life table method, and Kaplan–Meier survival curves were used to estimate the survival function. The log-rank test was used to test the association between study variables (gender, implant position, implant diameter, implant length, augmentation, oral surgeon) and time to event (i.e. implant failure). A binary logistic regression analysis (forward modelling – Wald) defining the patient as statistical unit was used to correlate the event biological complications with the following factors: gender (male/female), implant position (upper/lower jaw), augmentation (yes/no) and PI (<33%/≥33%). Odds ratio (OR) estimates and 95% confidence intervals (95% CI) were retrieved from the intercept of each factor.

Moreover, descriptive statistics were calculated for PI, BOP, PD and MR values. The Wilcoxon signed-rank test was used for within group comparisons from baseline to 6, 12 and 24 months at the patient level. The alpha error was set at 0.05.

Results

No primary stability could be achieved in eight of 60 patients. Accordingly, a total of 52 patients received the final prosthetic reconstructions. During the course of the study, four patients were lost to follow-up. Demographic data of the remaining 48

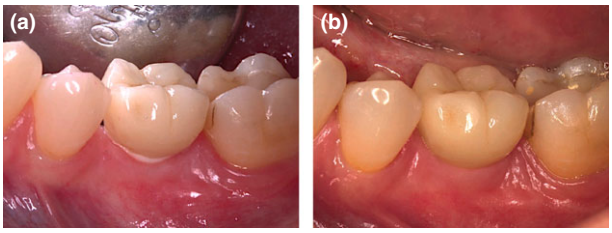

Fig. 2. Soft tissue wound healing. (a) Baseline situation after crown cementation revealed a soft tissue dehiscence at the buccal aspect. (b) Situation at 18 months showing a creeping attachment and complete soft tissue coverage of the exposed implant neck.

patients are presented in Table 1. Target implants were mainly placed in the lower jaws (72.9%), and most frequently revealed a diameter of 5.0 mm (64.6%) and length of 11 mm (93.8%). Multiple implants were only provided in 15 patients (31.3%), with a frequency of 20.8% for two implants and 10.4% for three implants. A simultaneous grafting of buccal dehiscence-type defects and internal sinus floor elevation was indicated at 25.0% and 12.5% of the target implant sites. An external sinus floor elevation and staged implant placement were accomplished in one patient (2.1%). The mean observation time was 25.5 ± 5.8
months (Table 1).

The postoperative wound healing was considered as generally uneventful in all patients (Fig. 2). No complications such as allergic reactions or abscesses were noted throughout the study entire period.

Implant survival and study variables

A total of two target implants in two patients were lost after a functioning time of 8 months. The cumulative survival rate was 95.8%, and the mean survival time amounted to 32.9 months (Fig. 3a). Even though both patients were male and both implants revealed a diameter of 5.0 mm, a length of 11 mm and were located in the lower jaw, the log-rank test failed to reveal a significant association between implant survival and gender ($P = 0.054$), implant diameter ($P = 0.290$), implant length ($P = 0.934$) or implant position ($P = 0.384$). Similarly, implant survival was also not influenced by the need of an augmentation procedure ($P = 0.761$) (Fig. 3b–f). However, a significant association was noted for the study variable oral surgeon ($P = 0.047$; log-rank test) (Fig. 3g).

Clinical measurements and biological complications

Mean PI, BOP, PD and MR values at baseline, 6, 12 and 24 months at the patient level are summarized in Table 2. In particular, mean PI values obtained at baseline slightly increased over time and reached statistical significance at 24 months ($P < 0.001$; Wilcoxon signed-rank test). Mean BOP values significantly increased at 6 and 12, respectively ($P = 0.004$, $P < 0.001$; Wilcoxon signed-rank test, respectively).

According to the given definition, 18 patients were diagnosed for initial peri-implantitis between 12 and 24 months. The Kaplan–Meier estimates of biological complications amounted to 37.5%.

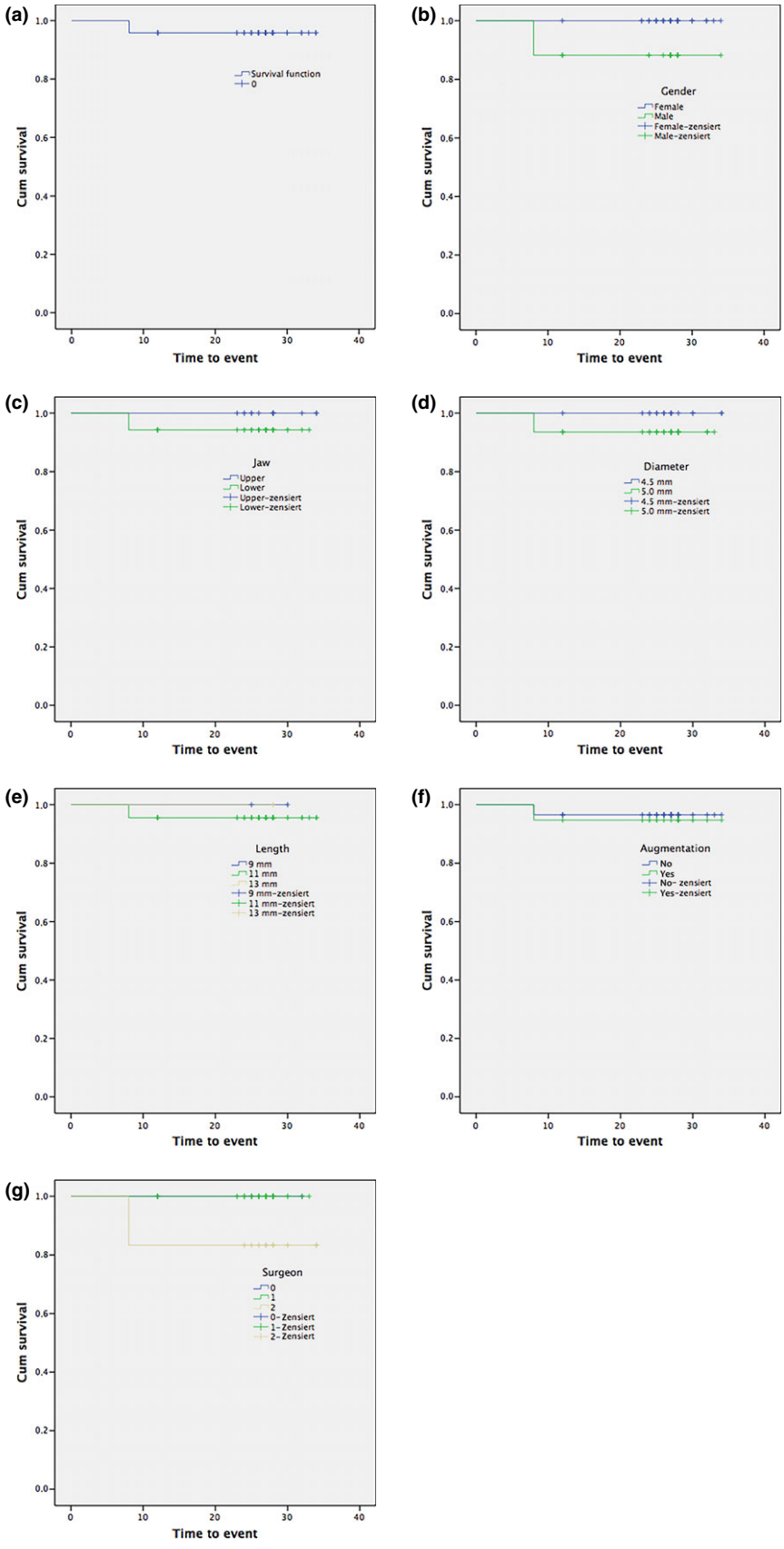

Fig. 3. Kaplan–Meier survival curves. (a) Cumulative survival rate. (b) Cumulative survival rate – factor gender. (c) Cumulative survival rate – factor jaw. (d) Cumulative survival rate – factor implant diameter. (e) Cumulative survival rate – factor implant length. (f) Cumulative survival rate – factor augmentation. (g) Cumulative survival rate – factor surgeon.

Table 2. **Clinical parameters (mean ± SD and median) at baseline, 6, 12 and 24 months (*n* = 48/46/45 patients)**

	Baseline		6 months		*P**	12 months		*P**	24 months		*P**
Plaque index	0.08 ± 0.24	0.0	0.05 ± 0.14	0.0	0.964	0.04 ± 0.14	0.0	0.464	0.34 ± 0.41	0.2	<0.001
Bleeding on probing (%)	21.3 ± 26.2	25.0	38.3 ± 27.5	25.0	0.004	64.1 ± 27.2	75.0	<0.001	13.9 ± 15.7	0.0	0.158
Probing depth (mm)	1.8 ± 0.7	1.7	2.3 ± 0.7	2.2	0.002	2.8 ± 0.7	2.7	<0.001	3.1 ± 0.5	3.2	<0.001
Mucosal recession (mm)	0.2 ± 0.3	0.0	0.1 ± 0.2	0.0	0.705	0.1 ± 0.2	0.0	0.737	0.0 ± 0.1	0.0	0.027

*Within group comparisons (Wilcoxon signed-rank test) at $P < 0.05$.

These patients were assigned to non-surgical treatment procedures (data on the clinical efficacy of therapy will be presented elsewhere). At 24 months, these interventions were associated with a marked reduction of mean BOP scores, almost reaching the baseline values ($P = 0.124$; paired *t*-test). Mean PD values significantly increased at 6, 12 and 24 months ($P = 0.002$, $P < 0.001$, $P < 0.001$; Wilcoxon signed-rank test) (Table 2). In all patients investigated, MR values decreased over time, even reaching statistical significance at 24 months ($P = 0.027$; Wilcoxon signed-rank test) (Table 2). In patients exhibiting a mucosal recession at baseline, this creeping attachment resulted in an almost complete coverage of the former soft tissue defect area (Fig. 2).

The binary logistic regression analysis failed to identify any significant correlations between the event biological complications and the factors investigated ($P > 0.05$, respectively).

Matrix metalloproteinase-8

The frequency of aMMP-8 levels <8 ng/ml (no inflammation), 8–20 ng/ml (mild inflammation) and >20 ng/ml (severe inflammation) was 37.5% (18 sites), 31.3% (15 sites) and 29.2% (14 sites) at 6 months, respectively. These frequencies were 20.8% (10 sites), 25.0% (12 sites) and 45.8% (22 sites) at 12 months and 25.0% (12 sites), 29.2% (14 sites) and 33.32% (16 sites) at 24 months (Table 3).

Mechanical and technical complications

Over the entire observation period, mechanical complications were only observed in 1 patient. At 23 months, a fracture affected the fibreglass abutment of the respective target implant. This was also associated with a technical complication (i.e. fracture) of the cemented crown. The Kaplan–Meier estimates of mechanical and technical complications amounted to 2.1%. The fibreglass fragment could be removed and a new prosthetic restoration cemented, which was successful during the further follow-up.

Discussion

The present prospective cohort study was designed to investigate the clinical performance of customized two-piece zirconia implants restored with cemented fibreglass abutments and all-ceramic crowns in the posterior mandible and maxilla. The statistical analysis has pointed to a high cumulative survival rate of 95.8% and a mean survival time of 32.9 months. Implant survival was neither affected by gender nor by implant diameter, implant length, implant position or augmentation thus indicating that this particular system may be safely used in any of the clinical indications investigated. Moreover, mechanical and technical complications were only observed at one target implant and therefore underline the stability and clinical applicability of the fibreglass abutments. Basically, the survival rates noted in the present study are within the range of those data reported in a recent retrospective analysis of ZV3 implants (Brüll et al. 2014). In particular, the cumulative survival rate of 55 one- and 66 two-piece implants that were inserted in a total of 74 partially edentulous patients and mainly (82.6%) restored with all-ceramic crowns amounted to 96.5% after 3 years. Unfortunately, the outcomes were not stratified for implant type (Brüll et al. 2014). Moreover, the present survival rates also corroborate recent prospective studies on single-tooth replacements by surface-modified one- (Oliva et al. 2010; Borgonovo et al. 2011; Cannizzaro et al. 2012; Kohal et al. 2012) and two-piece zirconia implants (Cionca et al. 2014; Payer et al. 2015). In particular, after an observation period of 24 months, the reported survival rate for two-piece zirconia implants amounted to 93.3%, while this value was 100% for titanium implants (Payer et al. 2015). In contrast, Cionca et al. (2014) reported on a lower cumulative survival rate (87%) at 1 year after loading of two-piece zirconia implants restored with cemented zirconia abutments and full-ceramic crowns. Implant failures were mainly attributed to an "aseptic" loosening (Cionca et al. 2014). A 2-year clinical study on 26 one-piece zirconia implants placed in a total of 16 patients reported on a survival rate of 96.16% (Borgonovo et al. 2011). A similar cumulative survival rate of 95.4% at 1 year was also noted after an immediate temporization of one-piece zirconia implants (Kohal et al. 2012). However, the failure rate (12.5%) was obviously higher for immediately loaded one-piece zirconia implants placed in postextraction sites (Cannizzaro et al. 2012). All these recently published data taken together with the results of the present study point to high survival and low complication rates of surface-modified zirconia implants used for single-tooth replacements. However, time to loading, including temporization of the implant during the initial healing period, should be critically considered and its impact on the outcome of therapy needs to be carefully addressed in future studies. When further analysing the present data, it was also noted that 18 patients were diagnosed for peri-implantitis after an observation period of 12.3 months, corresponding to a biological complication rate of 37.5%. The bivariate linear regression analysis failed to identify any correlation with the independent factors investigated. In this context, however, it must also be emphasized that the respective target implants merely revealed minor crestal bone level changes not exceeding the upper 25% of the implant length. This observation was supported by the moderate PD values noted at these sites. A recent retrospective

Table 3. **Frequency distribution of MMP-8 levels at 6, 12 and 24 months**

	6 months	12 months	24 months
No inflammation	18 (37.5%)	10 (20.8%)	12 (25.0%)
Mild inflammation	15 (31.3%)	12 (25.0%)	14 (29.2%)
Severe inflammation	14 (29.2%)	22 (45.8%)	16 (33.3%)
Not analysed	1 (2.1%)	4 (8.3%)	6 (12.5%)

aMMP-8: no inflammation (<8 ng/ml); mild inflammation (8–20 ng/ml); severe inflammation (>20 ng/ml).

analysis reported on similar PD values (range 1.0–3.0 mm) and marginal bone level changes (range 1.2 to −2.0 mm) for one- and two-piece ZV3 implants after a mean follow-up period of 18 months (Brüll et al. 2014). Moreover, several studies also reported on a pronounced bone loss at zirconia implants during the remodelling phase (Cannizzaro et al. 2012; Kohal et al. 2012; Payer et al. 2015). In particular, the mean radiographic bone loss adjacent to one-piece implants after 1 year amounted to 1.31 mm, but about 34% of the implant sites had lost at least 2 mm, and 14% even more than 3 mm (Kohal et al. 2012). As the present study did not consider the longitudinal assessment of interproximal radiographic bone level changes, it is impossible to estimate to what extend a more pronounced remodelling process may have contributed to the incidence of biological complications. However, the immunological analysis has pointed to elevated aMMP-8 levels over the entire observation period of 24 months. Previous studies provide some evidence that aMMP-8 is associated with the extracellular degradation of collagen and is positively correlated with plaque scores at mucositis sites (Basegmez et al. 2012; Schwarz et al. 2014). As PI values were not increased after 6 and 12 months of healing, it seems to be rather unlikely that the elevated BOP and aMMP-8 levels were caused by bacterial plaque biofilms. In this context, it must also be emphasized that the slight surface roughness of the transmucosal aspect of ZV3 implants may have no major impact on the microbial colonization of the peri-implant area (Bollen et al. 1996).

As aMMP-8 has also been shown to modulate the collagen metabolism of the oral mucosa (Korpi et al. 2009), one may speculate that the elevated values were associated with the marked increase of the vestibular mucosal level and gain of keratinized tissue as noted over the entire observation period of 24 months. To clarify this issue, the remodelling of soft- and hard tissues adjacent to zirconia implants needs further investigation.

Within the limitations of a prospective cohort study, it was concluded that this two-piece zirconium implant/fibreglass abutment system can be successfully used in the clinical indication investigated.

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Conflict of interests

The authors declare that they have no conflict of interests related to this study.

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