Immediate fixed rehabilitation supported by axial and tilted implants of edentulous jaws: a prospective longitudinal study in HIV-positive patients

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ABSTRACT

Aim The purpose of this study is to evaluate the success of implant prosthetic rehabilitation “All on four” in HIV positive patients.

Materials and Methods HIV-positive patients under a strict medical control with edentulous mandible and/or maxilla, were enrolled for the present study. The “all on four” protocol was applied with immediate fixed rehabilitations. Marginal bone loss, implant and prosthetic failure, biological and mechanical complications, serological levels (CD4 cell count, CD4/CD8 ratio and HIV-RNA) were recorded at 6, 12 and 24-month follow-up.

Results A total of 108 implant were placed in 21 patients, and 27 rehabilitations were delivered. Five implants were lost (survival rate = 95.37%). At the 24-months radiographic evaluation, perimplant crestal bone loss averaged 0.98 ± 0.21 mm for upright maxillary implants (n = 30 implants) and 0.87 ± 0.18 mm for tilted maxillary implants (n = 30 implants). In the mandible, a mean peri-implant crestal bone loss of 0.88 ± 0.32 mm for upright implants (n = 24) and 0.91 ± 0.30 mm for tilted implants (n = 24) was found. No statistically significant difference in the marginal bone loss between tilted and axially placed implants, and between jaws at 6, 12 and 24-month follow-up evaluation (P>0.05). Moreover, not statistically significant linear correlations were found between serological levels and marginal bone loss.

Conclusions Within its limitations, the present study reported that the “all on four” protocol can be a suitable treatment option in immunocompromised but immunologically stable HIV positive patients.

INTRODUCTION

HIV infection is a global pandemic, especially in developing countries, massively impacting on world public health. HIV is the virus responsible for a progressive immunodeficiency that weakens the body’s defense against pathogens and can be detected by a decreasing CD4+ cell count, indicator of the state of the disease. HIV-positive patients tend to develop more easily opportunistic infections and other HIV-associated oral lesions such as oral candidiasis, hairy leukoplakia, HIV associated gingivitis and periodontitis, Kaposi Sarcoma, non Hodgkin lymphoma, xerostomia and destructive carious disease (1), mostly due to poor oral hygiene and potentially also to alterations in the salivary flow. Atypical periodontal necrotic ulcerations and an increased incidence of herpetic infections have also been documented (2). Recently, thanks to highly active antiretroviral therapies, the life expectancy of HIV-positive patients has increased, their systemic health has improved and implant-supported prosthesis has become a valid alternative to removable prostheses in restoring dental aesthetics and function.

In a prospective cohort study (3) conducted at the IRCCS San Raffaele Hospital, Milan, it has been reported that implant prosthetic rehabilitation in HIV positive patients, showing strict adherence to antiretroviral drug regimen and good oral hygiene, is a reasonable treatment option with results slightly worse compared

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to the healthy population. 
In order to improve the quality of life and to encourage also a social rehabilitation of those patients, the "All on four" treatment concept represents a predictable procedure for the rehabilitation of completely edentulous jaws, showing the advantages of both the immediate loading, which allows immediate function, and full arch fixed prosthetic restoration, with a higher degree of patient satisfaction compared to removable prostheses (4) Low incidence of complications and high long-term survival rates with excellent Marginal Bone Level (MBL) outcome have been reported for this protocol by Paulo Maló et al. (2014) (5).

Early loss of the natural dentition due to oral complications and poor oral hygiene, often leads to a severe atrophy of the alveolar ridge (6). As a consequence, to achieve implant stability and support when rehabilitating atrophic edentulous jaws, an extensive surgical bone augmentation procedure, such as bone grafts or maxillary sinus elevation, would be required, resulting in higher risk of patient morbidity and complications, higher costs, longer time intervals and poor patient acceptance (7, 8). As HIV positive patients seem to have higher risk for both early and late postoperative complications, such as sepsis, oral and wound healing (9), they may benefit from a simpler and shorter treatment. Therefore a suitable option is the placement of four tilted implants – two most anterior placed axially and two posterior distally angled – according to “all on four” treatment protocol (10).

No significant differences in crestal bone loss and implant prosthetic failure rate have been found between tilted and axial implants (8, 11, 12). Tilted implants may achieve the same success rate as implants axially placed (13), showing both clinical and biological advantages, and cause no detrimental effect on the osseointegration process (14).

The purpose of this study is to evaluate the success of implant prosthetic rehabilitation “All on four” in HIV positive patients.

MATERIALS AND METHODS

Patient selection

This prospective longitudinal study was performed in the San Luigi Center for Infectious Diseases, IRCCS San Raffaele Hospital, Milan, Italy.

HIV-positive patients under a strict medical control and with severely resorbed mandible or maxilla, were enrolled from December 2013 to June 2014. The main inclusion criteria were patients with either edentulous jaws or jaws with teeth with a poor long-term prognosis treatment planned for extraction. The inclusion criteria were: age >18 years, total or partially edentulous in one or both jaws, adequate bone volume (divisions A, B, or C according to Misch classification of bone available) (15) and appropriate bone density (classes D1, D2, or D3 Misch) (16). Exclusion criteria were: severely immunocompromised patients with a high recurrence of opportunistic infections, tuberculosis, or malignancy, decompensated diabetes, severe malocclusion, severe parafunctions (bruxism), inadequate bone volume (Division D of Misch), inadequate bone density (density D4 Misch), disorders that contraindicate surgical procedures, lack of collaboration, lack of oral hygiene (plaque index higher than 1).

Diagnosis was made clinically and radiographically. All patients gave written informed consent, and underwent oral hygiene, conventional impression for study model for the fabrication of temporary prosthesis, panoramic radiographs and CT-scans before surgery.

Surgical procedure

One hour before the surgery patients were administered 2 g amoxicillin + clavulanic acid (Augmentin, GlaxoSmithKline, Belgium), which they continued (1 g twice a day) for 1 week after surgery. Implant surgery was performed under local anaesthesia (optocaine 20 mg/ml with adrenaline 1:80000, Molteni Dental, Firenze, Italy).

In edentulous mandibles, incisions were made on top of the alveolar crest, from the first molar on one side to the first molar on the contralateral side with bilateral releasing incisions. Subperiosteal dissection on the lingual and vestibular surfaces was carried out and mental foramina were located. Soon before implant placement, all compromised teeth with a poor prognosis were atraumatically extracted, when present, and sockets were carefully debrided. The four implants and abutments were placed starting with the posterior ones. Bilaterally the most posterior implants were placed close to the anterior wall of the mental loop and were tilted distally about 25–30 degrees in relation to the occlusal plane. The lower corner of the implant neck was positioned at bone level. Posterior implants were placed emerging at the second premolar position.

In edentulous maxillae, incisions were made on the alveolar crest from the first molar to the contralateral side with bilateral releasing incisions. Subperiosteal dissection was carried out. The most posterior implants were placed distally tilted approximately 25 to 30 degrees.

The diameter of the final drill was chosen based on the bone quality in order to optimize implant stability.

Implant placement was performed following the manufacturer’s instructions (TTx system, Winsix, Biosafin, Ancona, Italy), except that under preparation was used to achieve an insertion torque at least 35 Nm before final seating of the implant. Under preparation was performed in soft bone to obtain high primary...
stability. The implant neck was aimed to be positioned at bone level and bicortical anchorage was established whenever possible. The posterior implants were 3.8 or 3.3 mm in diameter and 15 or 13 mm in length, and the anterior implants were either 3.8 or 3.3 mm in diameter and 11 or 13 mm in length (TTx system, Winsix, Biosafin, Ancona, Italy).

Angulated abutments (Extreme Abutment, EA® Winsix, Biosafin, Ancona, Italy) for anterior implants were set at either 17° and those for posterior implants at 30° to compensate for the lack of parallelism between implants as well as to place the prosthetic screw-access holes in an occlusal or lingual location.

Flap adaptation and suturing were performed in the usual manner with 4–0 nonresorbable suture (Vicryl; Ethicon, Johnson & Johnson, New Brunswick, NJ, USA). After surgery were prescribed as postoperative care for all participants, non-steroidal anti-inflammatory drugs (Brufen 600 mg, Abbott Laboratories, Chicago, IL, USA), and chlorhexidine digluconate 0.2% mouthwash during the first 2 weeks. All patients were instructed to avoid brushing and any trauma to the surgical site and were recommended to follow a soft diet (avoiding bread and meat) for 2 months.

Prosthetic protocol

Provisional full-arch all-acrylic prostheses were delivered on the day of surgery, thanks to former impression taking. Pickup impressions (Permadyne, ESPE, Seefeld, Germany) of the implants were made at the conclusion of the surgery, after suturing, to manufacture a high-density all-acrylic prosthesis with titanium cylinders. No later than 3 h after the surgery an acrylic provisional prosthesis was delivered.

Articulating paper (Bausch Articulating Paper, Nashua, NH, USA) was used to check the occlusion and adjust it, if necessary. Static occlusion consisted of central contacts established on all masticatory units. Dynamic occlusion included canine/premolar guidance during lateral movements, regardless of the opposite arch settings. Screw access holes were covered with provisional resin (Fermit, Ivoclar Vivadent, Naturno, Bolzano, Italy). Final prostheses were delivered 4 months postsurgery. They were made of acrylic resin masticatory surfaces, and metal frameworks for increased strength and rigidity.

Follow-up

Follow-up visits were performed at 3, 6, 12 and 24 months after implant insertion with radiographic assessments to evaluate the marginal bone loss and the overall bone level.

According to the Infectious Disease Unit, Serological parameters (CD4 cell count, CD4/CD8 ratio and HIV RNA viral load) were assessed every 6 months. Each 6 months from implant placement, a dental hygienist performed oral hygiene procedures and clinical parameters regarding (15).

The surgical criteria used to evaluate the outcomes were the failure of the implant, absence of periimplantitis, absence of implant mobility, absence of mucosal suppuration and absence of pain at the time of examination. Restoration success was defined as the absence of fractures of the acrylic resin superstructure.

Radiographic examination

Intraoral digital radiographic assessments were made immediately after surgery and at each follow-up visit. Bone level measurements were performed on the mesial and distal aspect of each implant, using the implant-abutment junction as a reference point (15).

They were made perpendicular to the long axis of the implant with long cone parallel technique, using an occlusal custom template to measure the marginal bone level. A dedicated dentist measured the changes in crestal bone height over time. The difference in bone level was measured radiographically through specific software (DIGORA 2.5, Soredex, Tuusula, Finland). The software was calibrated for every single image using the known implant diameter at the most coronal portion of the neck of the implant. The linear distance between most coronal point of bone-to-implant contact and the coronal margin of the implant collar was measured to the nearest 0.01 mm, at both mesial and distal sides, and averaged. Bone level changes at single implants were averaged at patients level and then at group level.

Outcome measures

The outcomes were considered as follows: prosthesis failure, implants failure which led to implant removal (due to mobility, progressive marginal bone loss due to peri-implantitis, any mechanical complication rendering the implant not usable), biological and prosthetic complications (number and type were recorded as single episodes for each implant), peri-implant marginal bone level changes (MBLCs).

Statistical analysis

A dedicated software (SPSS 11.5.0, SPSS, Chicago, IL, USA) was used for all statistical analyses.

Data were analyzed at patient level and were reported and summarized as mean and standard deviations. For the outcome measures, the number of implant failures, prosthetic failures, peri-implantitis, occurrence of pus, pain, paresthesia, and fracture of fixtures were reported as absolute values and/or percentages in the whole sample (108 implants in 21 patients). In order to investigate the correlation between marginal bone levels and serological levels of CD4 cell count, CD4/CD8 ratio and HIV RNA at different time points (6, 12 and 24 months), a linear regression analysis was performed. The Pearson R coefficient was calculated and significance was set at p<.05. All results are provided as mean ±SD. To compare marginal bone levels at 6, 12 and 24 months between axial and tilted implants in maxilla and
mandible, a Student t test was applied at a significance level of $P = 0.05$.

**RESULTS**

A total of 108 implants were placed in 21 patients (Table 1). Among them, 11 were smokers (52.3%). Six patients received rehabilitation of both jaws, 9 patients received a maxillary rehabilitation and 6 received a mandibular rehabilitation (Table 1). All prostheses were supported by four implants. In total, 27 rehabilitations were delivered (Table 1).

**Implant failure**

Implant failure was registered in two patients (5 fixtures out of 108). Both patients were not smokers. One had suffered the loss of all implants due to late perimplantitis occurred 1 year after implant placement. The other patient lost one tilted implant as a consequence of a primary infection, at 2 months from placement.

The survival rate was 95.37% (96.30% for axial implants and 94.45% for tilted implants). Four implants out of 108 (3.70%) were lost for peri-implantitis in one patient and one implant out of 108 (0.93%) was lost for primary infection in another patient.

No fixture fracture occurred.

**Biological and prosthetic complications**

Biological and prosthetic complications were reported in Table 2. Peri-implantitis occurred in 4 implants in the same patient (3.70%), and resulted in the loss of the fixture and led to the removal of the implants (Table 2) and fixed prosthesis was lost (Table 2). Fracture of provisional prosthesis occurred in 2 patients (1 maxilla and 1 mandibular rehabilitations).

No paresthesia and no prosthetic complications in definitive prostheses were registered in the whole sample.

**Peri-implant MBLCs**

Marginal Bone Level (MBL) was followed up for 2 years (Table 3). At the 24-month radiographic evaluation, peri-implant crestal bone loss averaged 0.98 ± 0.21 mm for axial maxillary implants (n = 30 implants) and 0.87 ± 0.18 mm for tilted maxillary implants (n = 30 implants). In the mandible, a mean peri-implant crestal bone loss of 0.88 ± 0.32 mm for axial implants (n = 24) and 0.91 ± 0.30 mm for tilted implants (n = 24) was found.

No statistically significant difference in the marginal bone loss between tilted and axially placed implants, and between jaws at 6, 12 and 24-month follow-up evaluation (P>0.05) were recorded.

**Prosthetic failure**

One of the 27 fixed prostheses was lost during the observation period, representing a prosthetic survival rate of 96.3%. In definitive prostheses, no fractures of the acrylic resin superstructure occurred.

<table>
<thead>
<tr>
<th>Bone loss</th>
<th>UPRIGHT</th>
<th>TILTED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>maxilla n=30</td>
<td>mandible n=24</td>
</tr>
<tr>
<td>6 months (mm)</td>
<td>0.84 ± 0.21</td>
<td>0.80 ± 0.32</td>
</tr>
<tr>
<td>12 months (mm)</td>
<td>0.92 ± 0.36</td>
<td>0.85 ± 0.36</td>
</tr>
<tr>
<td>24 months (mm)</td>
<td>0.98 ± 0.21</td>
<td>0.88 ± 0.32</td>
</tr>
</tbody>
</table>

**TABLE 1** Implants dimensions and position

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Maxilla n=60</th>
<th>UPRIGHT n=30</th>
<th>13 mm</th>
<th>15 mm</th>
<th>11 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.3 mm</td>
<td>15</td>
<td>0</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.8 mm</td>
<td>10</td>
<td>0</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Maxilla n=48</th>
<th>TILTED n=30</th>
<th>3.3 mm</th>
<th>15 mm</th>
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<tbody>
<tr>
<td>3.8 mm</td>
<td>3</td>
<td>15</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Maxilla n=24</th>
<th>UPRIGHT n=24</th>
<th>3.3 mm</th>
<th>15 mm</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.8 mm</td>
<td>11</td>
<td>0</td>
<td>2</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Maxilla n=24</th>
<th>TILTED n=24</th>
<th>3.3 mm</th>
<th>11 mm</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.8 mm</td>
<td>2</td>
<td>11</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 2** Implant failure, prosthetic failure, biological and mechanical complications.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant failure</td>
<td>5</td>
<td>4.63%</td>
</tr>
<tr>
<td>Prosthetic failure</td>
<td>1</td>
<td>3.70%</td>
</tr>
<tr>
<td>Fixture fracture</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Perimplantitis</td>
<td>4</td>
<td>3.70%</td>
</tr>
<tr>
<td>Provisional prosthesis fracture</td>
<td>2</td>
<td>7.41%</td>
</tr>
<tr>
<td>Episode of Pus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pain</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**TABLE 3** Marginal bone loss at 6, 12 and 24 months from implant placement.
Serological parameters
Serological parameters are reported in Table 4. A not statistically significant linear correlation was found between:
- CD4 cell count and marginal bone levels at 6, 12 and 24 months (R=0.11, explained variance R²= 0.01);
- CD4/CD8 ratio and marginal bone levels at 6, 12 and 24 months (R=0.21, explained variance R²= 0.04);
- HIV RNA and marginal bone levels at 6, 12 and 24 months (R= 0.13, explained variance R²= 0.02).
All linear correlations were not significant (p>0.05).

DISCUSSION
The aim of this study is to investigate the survival rate of implants in “All on four” rehabilitations, performed on controlled HIV-positive patients with good oral hygiene. The recent switch of HIV infection from terminal to chronic disease has allowed HIV-positive patients to benefit from implant prosthetic rehabilitations, as their general health conditions and longevity improved. This explains why the current literature on this topic is considerably scarce and long-term clinical data are still lacking.
In 1998, Rajmay and colleagues (16) attempted the placement of one endosseous implant in a HIV-positive patient under strict medical control, obtaining good aesthetic and functional results after an observation period of 18 months. These findings have been supported by Strietzel et al. (17) who placed 10 implants in three HIV-positive patients with CD4+ cell counts >250/µL and viral load below the lower detectable limit. Their outcomes corroborate the hypothesis that implant-prosthetic rehabilitation of immunocompromised but immunologically stable patients can be a predictable treatment option.
In a prospective non-randomized clinical trial involving HIV-positive and negative patients requiring implant-supported mandibular overdenture, Stevenson et al. (18) reported osseointegration of all the implants, despite the high number of smokers included.
More recently Gherlone and colleagues (3) in a clinical trial, beside a cumulative implant survival rate of 92,11%, have showed a relatively high incidence of peri-implant infections in HIV-positive patients, occurred in the first 6 months after implant placement and probably due to individual susceptibility and immunological status. Therefore a strict protocol of infection control is needed when dealing with HIV-positive patients and the close collaboration with the Infectious Disease Department is essential for successful treatment outcomes, since the immune status and blood clotting parameters play a crucial role in patient selection.
Whether HIV-infected patients are more predisposed to experience postoperative complications from dental treatment is controversial. In a case report, Baron et al. (9) documented osseointegration in all implants placed in a HIV-positive patient: no signs of inflammation and uneventful healing of both the soft and the hard tissues were observed, supporting the hypothesis that minor surgery does not represent an increased risk for a controlled HIV-infected population. Same outcomes have been reported by Achong et al. (19) in a report on 3 cases. The authors assess also as the low CD4+ count levels at the time of implant insertion do not correlate with the outcome of the implants.
Other authors investigated the role of CD4+ cell count and its relation with implants survival. Oliveira et al. (20) in a pilot study, including 25 HIV-positive and 15 HIV-negative volunteers, showed high success rates without clinical complications for all implants placed in the study participants, and no statistically significant relationship between bone resorption and CD4+ cell count, viral load and type of ART.
In a recent study Gherlone et al. (21) evaluated the associations between implant survival and patient-related aspects such as smoking habits, oral hygiene, CD4+ level in patients with HIV infection. No significant associations were found between the considered variables, except for heavy smokers (>10 cigarettes/day) who showed to experience implant failures, perimplantitis, episodes of pus and pain more frequently compared with nonsmokers and light smokers (≤10 cigarettes/day).
Long-term success rates for implant prosthetic rehabilitations in HIV-positive patients have been reported by two studies (27, 28). Gay-Escoda and colleagues (27) registered implant survival and success rates of 98,3% and 68,4% respectively after 5 to 9 years of follow-up. Similarly, any evidence of an increased risk of implant failure after up to 10 years was found by Rania et al. (28), showing no significant difference in success rates between HIV-positive and HIV-negative patients.
According to the mentioned literature and the results obtained in the present study, successful implant survival rates in HIV-infected patients seem to be more related to proper patient selection, appropriate surgical

### Table 4: Serological levels at different time points (6, 12 and 24 months)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>6 months (mm)</th>
<th>12 months (mm)</th>
<th>24 months (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 cell count</td>
<td>536.33 ± 327.34</td>
<td>508.50 ± 288.03</td>
<td>531.17 ± 253.17</td>
</tr>
<tr>
<td>CD4/CD8 ratio</td>
<td>0.88 ± 0.37</td>
<td>1.05 ± 0.68</td>
<td>0.88 ± 0.76</td>
</tr>
<tr>
<td>HIV RNA</td>
<td>3.28 ± 9.52</td>
<td>14.62 ± 22.06</td>
<td>19.21 ± 16.73</td>
</tr>
</tbody>
</table>

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technique, meticulous follow up and strict antimicrobial protocol, rather than values of specific markers for HIV-positive individuals such as CD4+ cell count or viral load. Kolhatkar et al. (23) documented the successful placement of immediate implants into fresh extraction sockets in two HIV-positive individuals. The immediate placement reduces the total treatment time and allows to preserve the alveolar bone level from the collapse of healing events (24).

Immediate loading protocol was achieved in order to obtain immediate function, improving aesthetic outcomes8 and patient satisfaction. There are very few reports that show the clinical evidence of immediately loaded implants placed in HIV-infected patients. One of those (25) (Romano et al.) presents a fixed implant-supported immediate loading protocol in an edentulous asymptomatic HIV-positive patient, documenting the validity of this type of oral rehabilitation also in immunocompromised patients.

CONCLUSIONS

To our knowledge, the present study represents the only report on “All on four” implant prosthetic rehabilitation in HIV-positive population. Within its limitations, it shows how this protocol can be a suitable treatment option in immunocompromised but immunologically stable patients. However in the literature there is a lack of further long-term data and additional studies are needed.

REFERENCES


