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Title: Esthetic Outcomes of Single Immediate Implant Placement with Immediate Restoration Performed with Two Surgical Techniques

Abbreviated title: Esthetic Outcomes of Single Immediate Implant Placement

Research question(s):

1. Primary goal is to study the effect of the surgical technique (flap elevation or flapless) on the change in soft tissue (papillary height and facial margin level) between pre-operative level and up to 12-18 months following immediate implant placement and crown temporization.
2. Second goal is to study the effects of surgical technique (flap or flapless) and horizontal/vertical extraction socket dimensions on the lateral ridge dimensions and interproximal bone level adjacent to the implant 12-18 months following surgery.

Scientific abstract:

Immediate implant placement following tooth extraction has become a predictable method of therapy. Advantage of this method combined with immediate temporization, is evident in the maxillary esthetic zone, since it allows most continuous support of soft tissue contour. Surgical implant placement can be accomplished following elevation of a soft tissue flap or with a flapless approach. Numerous studies have demonstrated alveolar ridge remodeling with net bone loss at 6 months following elevation of flap (Schropp and Isidor, 2008, Buser et al., 2011). It is not clear, how this finding affects clinical changes in ridge dimensions (soft and hard tissue). Several uncontrolled trials have reported outcomes using the flapless technique (Raes et al., 2011, Van de Velde et al., 2010, Block et al., 2009), but no randomized controlled studies comparing these two methods are available. The aim of this study is to compare 1) the remodeling of the gingival tissue margin (change in papillary distance, gingival margin level / recession), and 2) the dimensional changes of the ridge and the stability of the radiographic alveolar bone level following immediate implant placement, temporization and restoration with or without flap elevation.

Lay abstract:

In implant dentistry, immediate implant placement is a reliable and predictable treatment. For patients who need implant therapy in the anterior region of the mouth, length of therapy and esthetic outcomes are of primary concern. Currently, one of the two surgical techniques are utilized for implant placement: flap elevation method or flapless method. However, there are no prospective longitudinal studies comparing the advantages and disadvantages of these two techniques on soft and hard tissue stability in the area. The aim of this study is to compare biological (soft and hard tissue remodeling) and esthetic outcomes of the two techniques.

Study Purpose and Rationale:

Introduction of the immediate implant concept is attributed to Schulte (1976). The earliest clinical case reports were published about 20 years ago (Lazzara, 1989, Ross et al., 1989). Today immediate implant placement has been established as a reliable and predictable therapy, with similar survival and success rates to delayed implantation (Schropp et al., 2003, Block et al., 2009). Survival rates for both procedures included in a recent systematic review exceeded

95% (Chen et al; 2009). Comparison of histological healing has demonstrated no significant difference in bone to implant contact in immediate and delayed implant placement (Paolantonio et al., 2001). Teeth scheduled for extraction and immediate implantation, as a result of extensive caries, endodontic failures, root perforations and fractures, often present with radiographic evidence of previous infections, in form of periapical radiolucency. No significant differences have been shown between implants placed in healthy versus previously infected extraction sockets, in terms of success and survival rates (Novaes and Novaes, 1995, Villa and Rangert, 2005, Lindeboom et al., 2006, Siegenthaler et al., 2007, Crespi et al., 2010, Waasdorp et al., 2010) and histological results (Novaes et al., 1998, Novaes et al., 2003, Shabahang et al., 2003, Chang et al., 2009), as long as the site is thoroughly debrided following removal of the tooth, primary implant stability is achieved, and in most cases, some type of antibiotic coverage is introduced.

Soft tissue dynamics following immediate versus delayed implant placement has been the subject of a recent systematic review, where risk indicators for gingival recession in conjunction with immediate implant placement included thin biotype, facial malposition of the implant and thin or damaged facial wall (Chen et al., 2009). Patient level satisfaction with esthetic outcomes in immediate implant placement was generally high, though a scarcity of studies evaluating objective parameters was evident. In a prospective case series of 35 immediate implants and immediate restorations followed for 12 months, mean in buccal and papillary soft tissue height were -0.55±0.53mm midbuccal and -0.53±0.39mm changes or less interproximal, with most of the difference between pre-operative levels to final measurements occurring prior to the permanent restoration of the implants at 6 months, resulting in later soft tissue stability and high patient satisfaction (Kan et al., 2003). A recent prospective, though not randomized, study of 16 immediate versus 23 conventionally placed implants demonstrated relative stability of the buccal margin up to 52 weeks following immediate implant placement and restoration, while the conventional, staged approach resulted in significant buccal recession, amounting to mean 1mm loss of midbuccal soft tissue height after one year of function (Raes et al., 2011). Moreover, in the immediate group, the flapless subgroup demonstrated significantly less recession than the flap subgroup at 26 and 52 weeks. Although a comparison between surgical techniques in immediate implantation was not the primary aim of this study, we are not aware of other published studies investigating the question. Therefore, we propose to conduct a study of the effect of the surgical technique (flap or flapless) on the change in soft tissue (papillary height and facial margin level) between pre-operative position and up to 12-18 months following surgery.

Intentional palatal orientation of immediate implants in maxillary anterior extraction socket or central to palatal orientation of immediate implant in bicuspid extraction socket usually results in a residual horizontal gap between the implant shoulder and the buccal aspect of the socket. This horizontal gap is referred to as Horizontal Defect Dimension (HDD). Width of HDD is dependent not only on the diameter of the extracted root at a given level and the position of the osteotomy, but also on the diameter of the selected implant to replace the tooth. The significance of the width of HDD on the healing has been addressed in numerous studies, with earlier studies suggesting threshold of 1.5mm or less (Akimoto et al., 1999, Wilson et al., 1998) for optimal bone to implant contact and, possibly, beneficial effect on osseointegration. Regenerative materials, bone grafts and barrier membranes, have been used in the past to address the gap between implant and bone at the time of immediate implantation, even in cases of intact buccal and interproximal bone levels, with rationale of epithelial exclusion from the

healing site, preservation of the ridge dimensions and maintenance of soft tissue stability (Chen et al., 2007, Araujo et al., 2011). However, a number of studies demonstrated successful immediate implant outcomes without use of grafting materials (Paolantonio et al., 2001, Covani et al., 2004, Sanz et al., 2010), including histological evaluation and confirmation of predictable new bone formation in HDD of up to 2 mm (Paolantonio et al., 2001). In addition, wider HDD (up to 3 mm) healing with new bone, following extraction and immediate implant placement has also been demonstrated in clinical studies (Schropp et al., 2003; (Botticelli et al., 2004). Favorable peri-implant soft tissue healing, including post-operative midfacial gingival margin and papillary height at 12 months, as well as high patient satisfaction were reported in a prospective study evaluating immediate implant placement and temporization, without utilization of grafts or barrier membranes (Kan et al., 2003).

Immediate implant placement does not preclude vertical and horizontal alveolar ridge loss following the extraction. In a study of hard tissue changes following immediate implant placement in 21 human extraction sites, significant postsurgical dimensional alterations were noted at 4 months following implant surgery (horizontal resorption amounting to 56% of the buccal bone and 30 % of the lingual bone), in spite of predictable new bone formation at the inner side of the extraction socket (Botticelli et al., 2004). Mucoperiosteal flaps were elevated in this study prior to extraction and implant placement. Elevation of full thickness flap induces accelerated bone remodeling of alveolar bone and net bone loss in the range of 0.5-1.0mm between 3 and 6 months following surgery (Donnenfeld et al., 1964, Wood et al., 1972, Pennel et al., 1967, Moghaddas and Stahl, 1980, Gomez-Roman, 2001). The question then arises, whether flapless immediate implantation will result in diminished horizontal bone loss, entailing enhanced ridge stability during the first 6 months following surgery. Therefore, the second aim of our study is to investigate the impact of surgical technique and extraction socket dimensions on the changes of the lateral ridge dimension and the interproximal bone level adjacent to the implant up to 12-18 months following surgery.

Summary of Study Purpose

1. To study the effects of the surgical technique on the soft tissue changes following extraction and immediate implant placement and temporization over a 12-18-month period.
2. To study the effects of the surgical technique and the horizontal/vertical defect dimension on the dimensional changes of the lateral ridge and the interproximal bone over a 12-18-month period.

Study Design and Statistical Procedures Overview

We propose to conduct a randomized controlled trial with two treatment arms: one in which immediate implant placement after tooth extraction is carried out after conventional mucoperiosteal flap elevation, and another that will adopt a flapless approach. Only maxillary teeth in the esthetic zone will be included. The primary outcome of the study is the gingival margin alterations at 12-18 months after surgery while the secondary outcome is the dimensional changes of the ridge at 12-18 months.

Power Calculations and Statistical Analysis

Based on similar data published in the literature, we have calculated that 17 subjects per group need to be recruited in order to have 80% power to detect a 0.5mm difference in soft tissue

changes between the two experimental groups. We plan to enroll a total of 40 subjects to account for potential dropout. Differences in the primary and secondary outcomes (changes in soft tissue, ridge dimension and bone level) overtime within each group will be examined as follows: continuous measurements will be summarized using mean/SD or median (interquartile range) for non-normal data. Differences between the two groups will be assessed using two sided t-test (means) or Wilcoxon Rank-Sum test (medians). Categorical measurements will be summarized using proportions. Differences between the two groups will be assessed using chi-square test or Fisher's Exact test for small counts.

Study Procedures

After informed consent is obtained, and initial periodontal therapy, whenever indicated, the scheduled extraction will be carried out without flap elevation, and the socket will be debrided meticulously. After verification that the local anatomical inclusion criteria are met, patients will be randomized to one of two treatment groups, a test (flapless group) and a control group (flap group). In the test group, the implant will be placed according to standard protocol at a position engaging the palatal wall without elevation of a mucoperiosteal flap In the control group, intrasulcular incisions will be carried out from one tooth distal to one tooth mesial to the extraction site and full thickness flaps will be elevated with periosteal elevator, including the papillae. The implant will be placed according to standard protocol at a position engaging the palatal wall, and the flaps will be sutured using a combination of interrupted and mattress sutures.

In both groups, temporary restorations will be delivered immediately after implant placement provided that the implant shows primary stability and has engaged in the bone with an insertion torque of 25Ncm or more (Norton, 2004). In case of a lower insertion torque, the protocol will be abandoned, a cover screw will be placed, and a two stage implant protocol will be followed. All patients will be advised to receive a permanent restoration 6 months after surgery, if the implant is deemed to be successful (Misch et al., 2008).

All patients will receive antibiotics 1 hour prior to surgery (Amoxicillin 1g; in allergic patients Clindamycin 300mg) and will continue with Amoxicillin 500mg (Clindamycin 150 mg) tid for seven days following surgery. All patients will be seen 1 week following surgery (suture removal visit, if applicable), review of OH; at two weeks following surgery, follow up of healing and OH; at 4 weeks, 6 weeks and 8 weeks (prophylaxis and measurements); at 3 months (prophylaxis and measurements); at 6 months (prophylaxis, measurements; removal of temporary restorations and impressions for permanent prosthesis,which will be delivered subsequently, can be done by restorative dentist or student at this visit or later) and at 12-18 months (prophylaxis, measurements).

Research Procedures

A reference notch will be made on the temporary crown with #1/2 bur at a 2 mm distance from the gingival margin at the mesiobuccal, midbuccal and distobuccal sites. The following measurements will be carried out:

1)Soft tissue distance from each of the three notches (mesiobuccally, midbuccally and distobuccally, respectively) at implant placement visit, following suturing, 4weeks, 6 weeks, 8 weeks, 3 months and 6 months. At 12-18 months these measurements will be performed using acrylic stent recoding previous reference points.

2a) Horizontal defect dimension (HDD) defined as horizontal distance from the implant shoulder to the alveolar socket wall, measured in 3 sites: mesial, buccal and distal; measured only at implant placement visit.

2b) Vertical defect dimension (VDD) defined as vertical distance from implant shoulder to the apical contact with the socket wall, measured in 3 sites: mesial, buccal and distal; measured only at implant placement visit.

2c) Buccal soft tissue and buccal plate thickness will be measured following the extraction using digital calipers (one measurement/ midbuccal/6mm apical to gingival margin); measured at implant placement only.

2d) Pocket depth (PD): pocket depth is defined as the distance from the gingival margin to the tip point of the probe (Williams probe). PDs will be measured at 6 sites per tooth, (mesiobuccal, midbuccal, distobuccal, distopalatal, midpalatal, mesiopalatal); measured before surgery and at 6months and 12-18 months.

2e) Buccal dimension of the ridge at the site of implant placement: measured after implant placement during surgery, at 3 months, 6 months and at 12-18 months.

2f) Impressions for study models will be taken first visit, following implant placement and temporization (on the day of surgery), at 8 weeks, 6 months and 12-18 months.

3) Interproximal bone level: a film holder with silicon putty to aid in reproducibility of the radiograph position will be used. The mesial and distal crestal bone level will be measured using the MIPACS software. Implant platform will serve as the reference point. Vertical and horizontal changes (depth and width of the vertical defect on the mesial and/ or distal aspect of the implant, if present) will be measured from radiographs taken at the time of completion of surgery, at 6 months and 12-18 months. Dose and frequency of x-rays in the study are standard of care for any implant patient in CDM or in standard clinical practice, and are not altered for the purpose of the study. (Medical status is updated and recorded at each CDM visit, including verification that female patients are not pregnant prior to x-ray taking; this is also standard of care).

4) The diameter of the apical radiolucency, when initially present, will be monitored /radiographically at will be assessed immediately after surgery at 6 months and at 12-18 months.

Study Instruments

We will use periodontal probe, used in routine periodontal therapy and caliper, used in restorative dentistry for linear distance measurements. Impressions and subsequent stone model construction are used routinely for diagnostic procedures in dentistry. Reproducibility of x-rays will be afforded by bite registration with impression putty, used in restorative dentistry. Changes on x-rays will be measured using MIPACS software, routinely used for dental patient care in CDM.

Additional Data Collection

Patients will fill out CDM medical and dental history forms, which will be reviewed orally as well, to identify inclusion criteria (patients over age of 18 years old, systemically healthy or controlled

common systemic conditions) and exclusion criteria (pregnancy, smokers over 10 cigarettes/day, parafunction or intent of orthodontic therapy).

Study Subjects

Forty subjects will be recruited among the patients attending the Clinic for Graduate Periodontics, College of Dental Medicine, Columbia University, who are in need of a tooth extraction at the maxillary premolar, canine and incisor region, and subsequent single implant placement. The reasons for extraction will include poor endodontic prognosis and/or non-restorable teeth (extensive caries, traumatic fractures, fractures of endodontically treated teeth, root perforation, root resorption, with or without radiographic periapical lesion up to 5 mm in diameter).

Inclusion Criteria

- Age 18 or older
- Systemically healthy patients or patients with controlled common systemic conditions (controlled hypertension, controlled diabetes HbA1c up to 7.5 %).
- Presence of both adjacent teeth
- Esthetically acceptable buccal gingival margin position prior to surgery, compared to neighboring teeth and contralateral tooth.
- Radiographic bone level distance from CEJ interproximally up to 5 mm.
- Location of buccal alveolar crest within 4 mm from the free gingival margin, verified after the extraction, before randomization; and fenestration, if present, up to 5mm in diameter at the apical part of the root and affecting less than 50% of the buccal socket wall.

Exclusion Criteria

- Pregnancy
- Current smoking exceeding 10 cigarettes/day
- Severe parafunctional habits
- Malocclusion or intent of orthodontic therapy in the future
- Teeth scheduled for extraction due to advanced periodontal disease

Recruitment

Forty subjects will be recruited among the patients attending the Clinic for Graduate Periodontics, College of Dental Medicine, Columbia University, who are in need of a tooth extraction in the maxillary premolar, canine and incisor region, and subsequent single implant placement. Patients will be screened by one of the investigators (Jaclyn Glick, Janet Stoupel and Panos Papapanou); only these investigators will be obtaining the informed consent form. If additional investigators will be included in the study, we will apply for an IRB modification prior to their participation in the study.

Confidentiality of Study Data

Patients are assigned identifying codes that are linked to all collected study data, stored in a secured database by the Primary Investigator. PHI/PII is not stored on a multi-user system, and PHI/PII is stored on an endpoint device that is password-protected and encrypted. The following individuals/ institutions/ representatives will have access to the records: the Principal Investigator and co-investigators, the FDA, the Department of Human Health and Human

Services agencies, the Columbia University/New York Presbyterian Hospital, including the Institutional Review Board, the implant company sponsoring the implants, Biomet 3i and it's representatives. Absolute confidentiality cannot be guaranteed because of potential need to share this information with the above parties. The aggregate results of this study, with preservation of patient confidentiality, may be used for teaching, meeting presentation or publishing purpose.

Location of Study

All therapy will be performed at the Postdoctoral Dental Clinics, College of Dental Medicine.

Potential Risks

1) Study related risks: Initial infection, pain or esthetically adverse outcome related to implant placement; inability to stabilize the implant due to poor quality of bone; implant failure and need for removal; discomfort in function and/or lack of satisfaction with the restoration for other reasons.
2) Protection against risks: All efforts will be made to minimize risks to all and every participant: only sites with healthy or almost healthy bone levels will qualify for the study to avert esthetic concerns, prophylactic antibiotics to prevent post-operative infection will be prescribed, restorative and functional expectations will be discussed and explained.

Potential Benefits

Patients will benefit from extraction of a tooth with hopeless prognosis, performed at no cost. They will benefit from the reduced cost of the implant and temporary restoration, that otherwise may not be available to them as option of therapy.

Alternative Therapies

Alternative Procedures:
1) not to replace the extracted tooth
2) to receive a removable partial denture to replace the missing tooth
3) to receive fixed crowns/bridge on adjacent teeth to replace the missing tooth
4) to delay implant placement for up to 6 months following extraction
5) not to have temporary crown made, following implant placement, but to have a removable temporary replacement. This option will be followed, if the implant does not attain initial stability of at least 25 Ncm.

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