Curriculum Vitae

Name: Frances Michelle Herrero Náter

Contact information: ferdifrances@gmail.com

Degree and Date to be Conferred: M.S., 2018

Collegiate Institutions Attended:

2015-*Present* University of Maryland Baltimore, School of Dentistry

Master of Science in Biomedical Science

Periodontics Resident, Certificate of Periodontology

2014-2015 General Practice Residency, Mount Sinai Hospital, New York, NY

2010-2014 University of Puerto Rico, School of Dentistry

Dental Medicine Doctor (DMD)

2006-2010 University of Puerto Rico, Mayagüez Campus

Bachelor of Science (B.S.) in Biology

Abstract

Title of Thesis: Improved oral health quality of life and satisfaction with implant-supported overdentures for patients with type 2 diabetes mellitus

Frances Herrero, Master of Science in Biomedical Science, 2018

Thesis Directed by: Dr. Thomas W. Oates

Diabetes mellitus has long been considered a contraindication to dental implant therapy dependent on glycemic control. Recent studies have suggested that the risks of implant therapy may be less than previously thought. However, the potential for benefit from implant therapy for patients with diabetes, especially for those individuals lacking good glycemic control, remains to be determined. The goal of this study was to examine the benefits of implant-supported mandibular overdenture therapy for patients with type 2 diabetes. A total of 157 patients, with and without diabetes received two anterior mandible dental implants (SLActive, Straumann, Basel, Switzerland) to support an implant overdenture (IOD). To assess benefits of care, patients completed an Oral Health-Related Quality of Life (OHRQoL) and a Patient Satisfaction questionnaire at baseline prior to implant placement, and six and twelve months after implant restoration. Venous blood samples to measure HbA_{1c} levels were taken at the same timepoints. Generalized estimating equations (GEEs) were used to compare the three groups and three periods (two factors). Multiple comparisons were addressed using the Bonferroni test. Patients were grouped according to glycated hemoglobin (HbA_{1c}) levels at baseline. Sixty-three patients had no diabetes diagnosis, 65 patients presented well-controlled diabetes ($6.1\% \leq HbA_{1c} \leq 8.1\%$) and 29 patients poorly controlled diabetes ($8.1\% \leq HbA_{1c} \leq 12.0\%$). Implant overdenture treatment resulted in significantly higher OHRQoL summary scores compared to baseline across all patient groups, with no differences

between groups. Similarly, general satisfaction (100mm VAS) was significantly increased from baseline 6 months following implant treatment, (39 mm higher, 95% CI: 32 to 47 mm). No statistically significant changes or improvement in HbA_{1c} were observed after treatment. The results demonstrate that patients with type 2 diabetes can benefit significantly from mandibular implant-retained overdentures independent of glycemic status.

Improved Oral Health Quality of Life and Satisfaction with Implant-Supported Overdentures for Patients with Type 2 Diabetes Mellitus

by
Frances Michelle Herrero Náter

Thesis submitted to the Faculty of the Graduate School of the
University of Maryland, Baltimore in partial fulfillment
of the requirements for the degree of
Master of Science
2018

Table of Contents

List of Tables

List of Figures

I. Introduction

A. Background and Rationale

Diabetes mellitus includes a group of metabolic diseases that affects 30.3 million individuals, or 9.4% of the U.S. adult population (CDC 2017). By 2030, the prevalence of type 2 diabetes is projected to have increased by 69% in developing countries and by 20% in developed countries because of population growth, aging populations and urbanization-associated lifestyle changes (Shaw at el., 2010). The World Health Organization (WHO) predicts that 439 million people worldwide, almost 10% of adults, will suffer from diabetes by 2030 (WHO 2011).

Type 2 diabetes mellitus is the most commonly diagnosed form of diabetes. Its complications significantly impact quality of life, longevity and healthcare costs. Periodontitis is well recognized as a complication of diabetes, with the risk of developing periodontitis is at least three times greater in individuals presenting type 2 diabetes mellitus (Mealey et al., 2006.) Periodontal disease, the sixth-most prevalent chronic condition in the world, is a microbial biofilm-initiated, host-mediated, disruption of soft and hard tissues supporting the teeth (Hajishengallis et al., 2012; Kassebaum et al., 2014). If untreated, periodontal disease can ultimately lead to tooth loss and functional compromises (Buckley et al., 1984).

Several large clinical trials have shown that the complications of hyperglycemic conditions are directly proportional to glycemic levels as measured with glycated hemoglobin (HbA1c; DCCT, UKPDS). These studies support HbA1c levels of less than 6.5-7% as therapeutic goals for well-controlled diabetes. The UKPDS study reported a long-term difference between mean HbA1c levels of 7.0% and 7.9% relative to diabetic

complications. However, several studies have suggested that the risk of microvascular complications does not rise considerably until HbA1c levels are greater than 8% (DCCT, 1993).

Compromises in oral health, such as tooth loss and edentulism, have been shown to adversely affect individual quality of life. This may be of greater importance for patients with diabetes, who are critically dependent on dietary management of their diabetic condition. Tooth loss may be impactful for these patients in part by discouraging a healthy diet, with ramifications on glycemic control (Azogui et al., 2017). Consequences of tooth loss include difficult chewing and speaking, esthetic dissatisfaction and social stigma (Patel et al., 2013). Research has found an association between tooth loss and lower consumption of dietary fiber, fruits and vegetables, as well as high intake of cholesterol and saturated fatty foods (Sheiham et al., 2001).

The prevalence of edentulism increases with age. According to the National Health and Nutrition Examination Survey (NHANES), the prevalence of edentulism was nearly 19% among people 65 years and older during the years 2011-2012. Edentulism was twice as prevalent among adults aged 75 and over (26%) compared with adults aged 65–74 (13%). Together, these findings reinforce the increased risk for edentulism as patients age, which corresponds directly with the increasing risks for diabetes and its complications as patients age.

To understand the association between diabetes and tooth loss in the United States, an analysis of data from the NHANES 2003-2004 reported a prevalence of edentulism of 28 percent and 14 percent among people with and without diabetes, respectively. The prevalence of edentulism was significantly higher among people with

diabetes (Patel et al., 2013). Supporting this increased risk, an animal study found using 16S rRNA sequencing that diabetes causes a shift in oral bacterial composition and, by transfer to germ-free mice, that the oral microbiota of diabetic mice is more pathogenic (Xiao et al, 2017). Nevertheless, a recent cross-sectional study revealed the relationship between systemic inflammation and periodontitis in patients with cardiovascular disease and found that diabetes mellitus was negatively associated with number of remaining teeth, but it was not correlated with C-reactive protein levels and antibody titers. Thus, DM might affect periodontitis-induced tooth loss but may not directly influence systemic inflammatory reaction and antibody titers; these might be dependent on dentate and edentulous state (Aoyama et al., 2018).

Thus, partial and complete edentulism in the diabetic population is concerning because it may affect the individual's ability to maintain a healthy diet due to a decreased chewing efficiency, which eventually may have a negative impact on glycemic control (Kawamura et al., 2001; Nuttall et al., 2003).

B. Diabetes and Dental Implants

Diabetes mellitus remains one of the most commonly encountered contraindications to dental implant therapy. Patients with good glycemic control have been considered acceptable candidates for implant therapy, while those lacking good glycemic control have often been denied the benefits of implant therapy (NIH 1988). However, recent studies have demonstrated that high success rates are achievable in diabetic patients independent of glycemic status (Oates et al., 2013, 2014; Dowell et al., 2007; Oates et al., 2009; Khandelwal et. al, 2013, Eskow and Oates 2016). Taken

together, these studies demonstrate that the risks for implant therapy may not be as great as previously thought. With the increased risk for tooth loss in patients with diabetes, and diminished concern for risks for implant therapy, proper application of implant therapy for patients with diabetes may now focus on the potential for benefits from this therapeutic approach.

C. Oral Health Impact Profile (OHIP) and Implant Supported Overdentures (IOD)

The Oral Health Impact Profile was developed from a model of oral health status (Locker et. al, 1998). It is a 49-item profile that defines the impacts of oral health conditions on aspects of function, daily living and social interactions in seven domains, including functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap (Slade et. al, 1994). The OHIP is the most extensively studied oral health-related quality of life scale now translated into over 20 languages (Lawal, 2014). A valid and sensitive 20-item short form of the OHIP was developed specifically for dentures (Allen et. al, 2002).

It has been recommended that the minimum standard for the treatment of the edentulous mandible should be a 2-implant overdenture (Feine et al., 2002; Thomason et al., 2012). Mandibular two-implant overdentures have been shown to be superior to conventional dentures in randomized and non-randomized clinical trials; participants are significantly more satisfied, they are more comfortable, speak more easily and ratings of quality of life have been significantly higher. A recent systematic review evaluating 53 studies found that treating complete denture wearers with implants led to obvious improvements of patients' satisfaction with regard to denture comfort, although not

always accompanied with improvement in general quality of life (QoL) and/or health related QoL. Even though patients could chew better, stronger and eat more tough foods, no changes in dietary intake, BMI and blood markers were seen (Boven et al., 2015). Authors did find that treating complete denture wearers with implants to support their dentures improved their chewing efficiency, increased maximum bite force and improved satisfaction.

With the recognized benefits of implant-supported dentures, the goal of the present study was to comparatively measure the benefits of implant-supported mandibular dentures compared to complete dentures in edentulous patients with type 2 diabetes across a broad range of glycemic levels.

II. Methods

This single-center, prospective, cohort study evaluated the effects of glycemic control on implant related outcomes in edentulous patients receiving mandibular implant supported overdentures. As part of the long-term evaluation of these patients, and the subject of the current report, this study also assessed the benefits of implant support on changes in oral health quality of life (OHIP) and general satisfaction for patients with and without type 2 diabetes over 1 year following implant-supported restoration. All patients were recruited at the School of Dentistry, University of Texas Health Science Center at San Antonio. Participants were enrolled from September 2007 through June 2012.

A. Inclusion Criteria

The study included edentulous patients 25 years or older, with or without type 2 diabetes, who needed treatment with two dental implants in the mandibular anterior region to support an implant-retained complete overdenture. Patients were grouped as "no diagnosis" if they denied a past diagnosis of diabetes mellitus. The diagnosis of type 2 diabetic patients was verified using the patients' medical records at time of enrollment. The glycemic control subdivisions were done using the HbA1c levels measured using a single Clinical Laboratory Improvement Amendments-certified commercial laboratory at baseline. Medical management of diabetes by means of diet, oral hypoglycemic agents, insulin or combination therapy was permitted. Patients' height, weight, waist circumference, and blood pressures were recorded.

Implant sites were limited to the anterior mandible (canine-premolar region) that presented enough bone volume to allow for the placement of 4.1-millimeter diameter implants with a length of 8 to 12 mm. Participation was also limited to sites that had a minimum of 4 months healing time post extraction prior to implant placement. Participants were also required to have acceptable complete maxillary and mandibular dentures for a minimum of 6 months.

B. Exclusion Criteria

Criteria for exclusion from the study included HbA1c levels greater than 12 percent at the time of screening and systemic conditions other than type 2 diabetes that were considered to be a contraindication to implant therapy. Patients were also excluded if they were receiving anti-resorptive drug therapy, pregnant, reported a smoking habit, had untreated oral infections, had a viral or autoimmune disease, or presented implant sites that underwent bone-grafting procedures involving use of autogenic or allogeneic materials within one year of the study or implant sites that had undergone alloplastic grafting procedures.

C. Implant Therapy

Two transmucosal dental implants [4.1-mm diameter and 8-, 10-, or 12-mm length, (SLActive, Straumann, Basel, Switzerland)] in the anterior mandible (canine and incisor region) were placed in each patient to support a mandibular overdenture. Implant length was determined by the surgeons at the time of the surgery; implants of the same length were placed bilaterally when existing bone dimensions were appropriate. Implants

were placed using standard surgical protocols by multiple clinicians, including residents and faculty members at UTHSCSA under the supervision of the primary investigator (PI; T.W.O.). The surgeon and PI made clinical assessments jointly regarding bone type at implant placement, according to a four-tiered scale: high density (type I), moderate density (type II), low density (type III), and very low density (type IV) [31 reference]. Following implant placement, transmucosal healing abutments were placed and adjustments were made to the denture base to eliminate any contact between the implant and denture. Post-operative prescriptions consisted of an antibiotic regiment consisting of amoxicillin (500mg) or clindamycin (150mg) three times per day for seven days and chlorhexidine gluconate (0.12 percent) mouthrinse twice a day for two weeks. Following a four-month healing period the two implants were restored with locator attachments to engage the denture base.

D. Study Procedures

Venous blood samples were taken by the examiners at the enrollment for measurement of HbA1c to determine eligibility for participation in the study. Blood draws were also taken within two weeks prior to or at implant placement (baseline), two months after surgery, and at implant restoration (four months after surgery), and three, six and twelve months after restoration.

E. Questionnaires

Subjects completed questionnaires in a secluded private room under the supervision of a trained research assistant.

- **Oral Health-Related Quality of Life-** Numerous indices have been developed to measure the impact of oral health on patients' lives (e.g., Atchison 1990; Cornell 1994). The Oral Health Impact Profile (OHIP) (Slade 1994), has been validated for English-speaking populations in Ontario, Australia and the UK, as well as for the French-Canadian and Swiss populations, an Argentine population, German, Dutch and others, including the Hispanic population in Texas. Being a multidimensional and generic measure of oral health outcomes, the OHIP has been shown to discriminate between the dentate and edentulous, and between subjects who do and do not wear dentures. Additionally, it was capable of detecting differences in the expected direction between groups for all domains tested in clinical trials of conventional and 2-implant supported overdentures (Heydecke 2003).
    - Patients were asked to respond to the 20-item OHIP questionnaire that consists of separate domains as described by Slade (1997). These comprised the seven subscales/domains originally purported for the OHIP, based on the Locker's structural model of oral health: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap.
    - Responses to each OHIP question, within the previously described seven subscales, were presented on a 6-point Likert scale (Box 1.) ranging from: 1 = always, 2 = most of the time, 3 = some of the time, 4 = occasionally, 5 = rarely, 6 = never. Lower scores would indicate more problems. A total OHIP score was obtained by summing up the scores for all of the domains. Patients were asked to

respond to the OHIP-20 at baseline (prior to implant surgery), and 6 and 12 months post-restoration.

Table 1. Separation of questions according to different subscales, representing the seven domains of Locker's model of oral health

Subscale	Acronym by Slade (1997)	Questions
S1, Functional Limitation	FL	1, 2, 3
S2, Physical Pain	P1	4, 5, 6, 7
S3, Psychological Discomfort	P2	8, 9
S4, Physical Disability	D1	10, 11, 12, 13
S5, Psychological Disability	D2	14, 15
S6, Social Disability	D3	16, 17, 18
S7, Handicap	H	19, 20

- **Patient Satisfaction** – The general satisfaction was evaluated with all aspects of treatment rated on 100 millimeters (mm) VAS. Subjects were asked to rate their perceptions or other factors that are important to them.

F. Statistical Analysis

The same strategy was used for all outcome variables, namely patient satisfaction items, OHIP-20 summary scores (overall and separate domain), and $HgA1_c$. Asymmetric distribution of data and heterogeneous variance precluded the use of parametric tests. Therefore, we used generalized estimating equations (GEEs) for comparing the three groups and three periods (two factors). Tests used assumed an exchangeable working correlation and used an identity link function with generalized score statistics. Multiple comparisons were performed by the Bonferroni test. Analyses were executed by SPSS 23 software.

Statistical assessment of separate dependent variables was interpreted in a hierarchical way. In other words, results for patient satisfaction were considered as a primary outcome variable, with other questionnaire items considered explanatory. The same approach was used for the OHIP-EDENT; summary scores were considered primary, whereas the seven separate OHRQoL domains had explanatory relevance. Therefore, based on the existence of two potentially correlated PRO, we considered α as 0.025.

For a better clarification of the impact of dental implants on glycaemia, analyses were repeated with five groups in the case of main patient-reported outcomes (general satisfaction and OHIP-EDENT – summary score), and $HbA1_c$.

III. Results

One hundred sixty-five patients were initially randomized into the study, of which 8 did not receive implant treatment. One hundred fifty-five completed the baseline, one hundred forty-one completed the 6-month, and one hundred thirty-seven completed the 12-month for the OHP surveys, while 141 completed the three general satisfaction surveys. The age of study participants ranged from 38 to 85 years of age, with a mean age of 64 years.

Within group comparisons

Table 2 shows the demographic information summarized with averages and percentages of the population.

Age	Sex	Weight (avg.)	Waist Circ.	BMI	Baseline HbA1c	Taking insulin	Taking Oral Diabetes Meds
64.1 ±9.2 years	53% female	193.7 ±47.6 lbs.	42.2 ±6.9 in.	31.9 ±7	6.8% ±1.5	20%	56%

Table 2. Demographic data (mean ± SD and/or %)

Patients were classified as being diagnosed with diabetes or not being diagnosed prior to study enrollment. The study population consisted of 94 patients (60%) who entered the study diagnosed as having type 2 diabetes and a mean HbA1c level of 7.4 ±1.6% and a minimum and maximum HbA1c level of 5.2% and 11.2%, respectively. The remaining 63 patients (40%) had no previous diagnosis of diabetes, had a mean HbA1c level of 5.7 ±0.3%, and a minimum and maximum level of 5 and 6.5,

respectively. Patients were placed into the previously defined groupings based on their HbA1c values. Figure 1 shows the distribution of HbA1c values amongst the study participants indicating that the majority of the participants in the study were within control group or the well-controlled diabetes group.

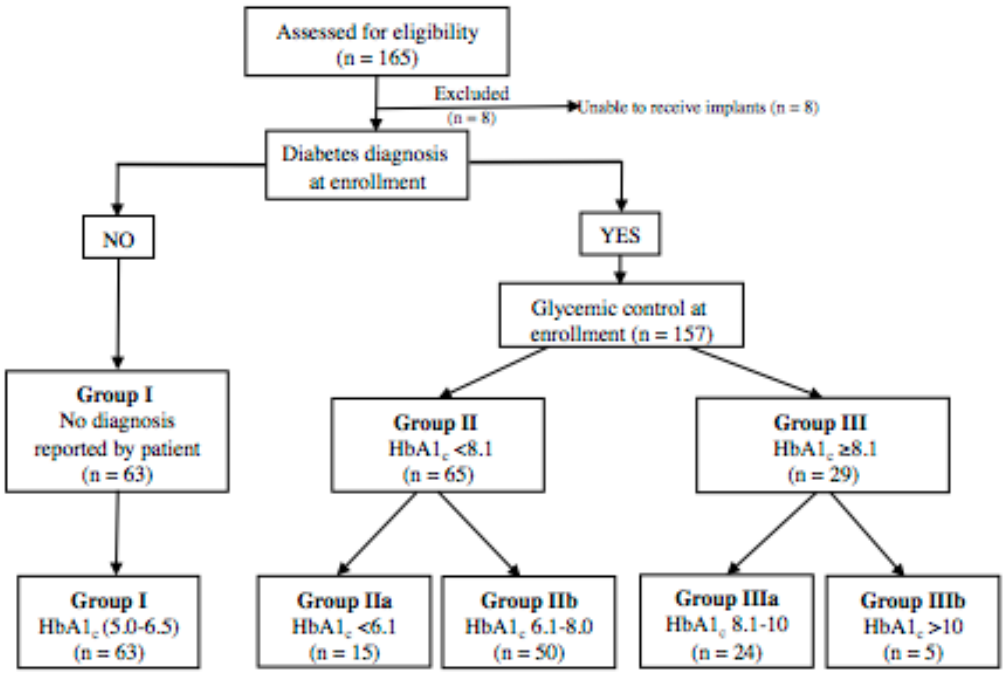

Figure 1. Distribution of HbA1c values amongst the study participants

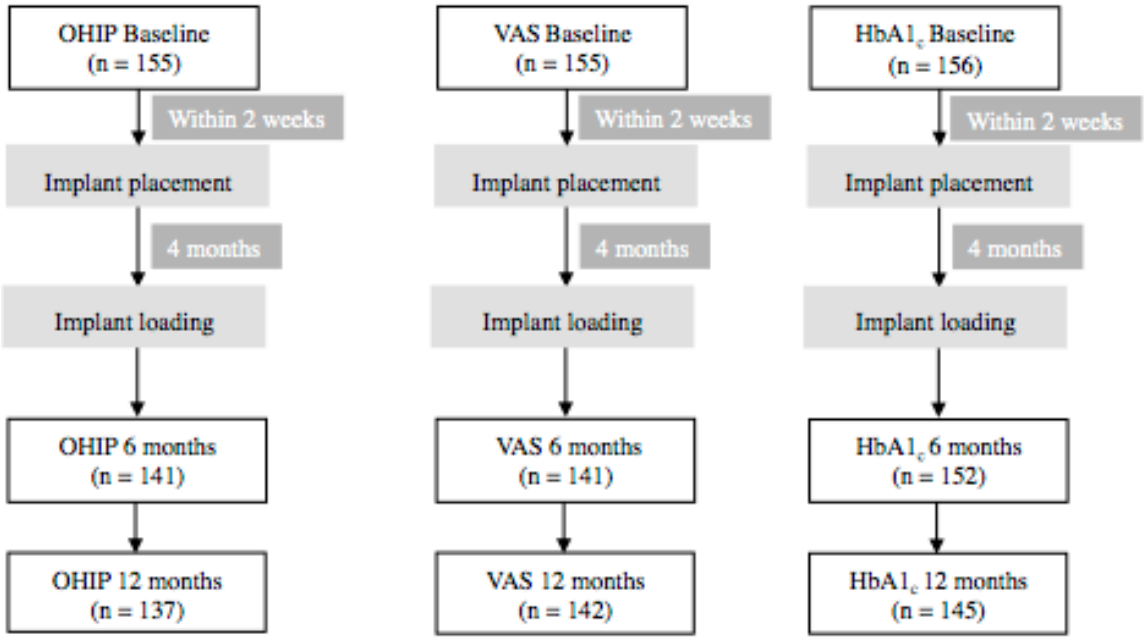

Figure 2. Number of participants at baseline, six months and twelve months

Between group comparisons

OHIP-20E

Treatment with implant overdentures resulted in significantly higher OHIP-EDENT summary scores compared to baseline, indicating an overall improvement in OHRQoL. There was no significant difference between the 6- and 12-mo. follow-ups. Overall summary score estimates were: 72.1 at baseline (95 CI: 67.5 to 77.0), 101.6 at 6 mo. (95 CI: 98.6 to 104.6), and 101.6 at 12 mo. (95 CI: 97.6 to 105.7). The same results were observed for all the seven separate domains, i.e. similar results on 6 and 12 mo., with a significant increase from baseline (Bonferroni test). Table 3 provides mean results for the OHIP-EDENT as well as the output of GEE.

Table 3. OHRQoL of participants – mean OHIP-EDENT scores (95% CI) by three groups and time period.

Component	Baseline	6 mo.	12 mo.	GEE, P Value		
				Groups	Time	Interaction
Summary score (TOTAL)						
Nondiabetic	71 (64, 79)	102 (98, 107)	102 (97, 107)			
HbA1c < 8.1	76 (69, 83)	100 (95, 105)	103 (97, 108)	0.780(ns)	<0.001*	0.388(ns)
HbA1c ≥8.1	69 (60, 80)	102 (96, 109)	101 (91, 111)			
Separate domains						
S1: FL (functional limitation)						
Nondiabetic	8 (7, 9)	13 (12, 14)	13 (12, 14)			
HbA1c < 8.1	9 (8, 10)	13 (12, 14)	13 (12, 14)	0.636(ns)	<0.001*	0.089(ns)
HbA1c ≥8.1	7 (6, 9)	14 (12, 15)	13 (12, 15)			
S2: P1 (physical pain)						
Nondiabetic	14 (13, 16)	20 (19, 21)	20 (18, 21)			
HbA1c < 8.1	15 (13, 16)	19 (18, 21)	20 (19, 22)	0.836(ns)	<0.001*	0.223(ns)
HbA1c ≥8.1	14 (12, 16)	20 (18, 21)	19 (17, 22)			
S3: P2 (psychological discomfort)						
Nondiabetic	7 (6, 8)	10 (10, 11)	10 (10, 11)			
HbA1c < 8.1	8 (7, 9)	10 (10, 11)	11 (10, 11)	0.302(ns)	<0.001*	0.433(ns)
HbA1c ≥8.1	7 (5, 8)	10 (10, 11)	10 (9, 11)			
S4: D1 (physical disability)						
Nondiabetic	13 (11, 15)	20 (19, 21)	20 (18, 21)			
HbA1c < 8.1	14 (12, 16)	20 (19, 21)	21 (20, 22)	0.662(ns)	<0.001*	0.595(ns)
HbA1c ≥8.1	13 (11, 15)	20 (19, 22)	20 (18, 22)			
S5: D2 (psychological disability)						
Nondiabetic	7 (6, 8)	11 (10, 11)	11 (10, 11)			
HbA1c < 8.1	8 (7, 9)	10 (10, 11)	10 (10, 11)	0.971(ns)	<0.001*	0.873(ns)
HbA1c ≥8.1	7 (6, 8)	11 (10, 11)	11 (10, 12)			

Table 3 Continued

S6: D3 (social disability)						
Nondiabetic	14 (13, 15)	17 (17, 18)	17 (17, 18)			
HbA1c < 8.1	14 (13, 16)	17 (17, 18)	17 (16,18)	0.840 (ns)	<0.001*	0.961 (ns)
HbA1c ≥8.1	14 (13, 16)	17 (17, 18)	17 (16, 18)			
S7: H (handicap)						
Nondiabetic	8 (7, 9)	11 (11, 12)	11 (11, 12)			
HbA1c < 8.1	9 (8, 10)	11 (11, 12)	11 (11, 12)	0.590 (ns)	<0.001*	0.655 (ns)
HbA1c ≥8.1	8 (7, 10)	11 (11, 12)	11 (10, 12)			

*significant effect; (ns)non-significant.

Patient satisfaction

Table 4 provides data on patient satisfaction with existing mandibular complete dentures. General satisfaction was significantly lower before implant treatment; at the 6-month follow-up, it was 39 mm higher (95% CI: 32 to 47 mm). Thereafter, general satisfaction underwent a non-significant reduction (mean difference, 6 to 12 months: -3 mm; 95% CI: -9 to 3 mm). Mean difference between the 12-month and baseline general satisfaction was 36 mm, with 95% CI ranging from 28 to 45 mm.

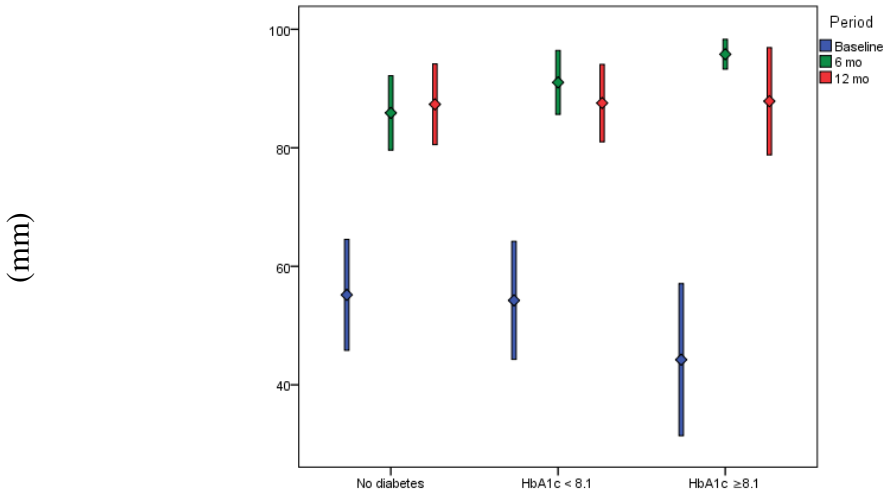

Figure 3. Mean values for the general satisfaction item (100-mm VAS) and 95% CI according to the three groups and periods.

In general, all items followed the same trend for between-time differences, i.e. baseline values were lower than post-treatment, but without significant difference between 6 and 12 months. A single exception was the item related to "speech". For that item, pairwise comparisons yielded significant differences, with a minor decrease from 6 to 12 months (-5 mm; 95% CI: -1 to -10 mm).

Although all between-time differences were significant, their magnitude ranged considerably among different satisfaction items. For instance, mean baseline to six-month improvements were dramatic for stability, which increased 51 mm (95% CI: 43 to 60 mm), as well as comfort, with more 39 mm (95% CI: 31 to 47 mm). At the other extreme is cleaning, with just 8 mm of change (95% CI: 3 to 14 mm); in other words, with unlikely clinical relevance. The same improvement was intermediate for speech (22 mm; 95% CI: 16 to 29 mm) and aesthetics (22 mm; 95% CI: 15 to 29 mm).

Group division did not influence general satisfaction, as well as the five related sub-items (cleaning, speech, comfort, aesthetics and stability). Likewise, group x time interactions were not significant for any of the six items.

Table 4. Mean values for the satisfaction questionnaire (95% CI) according to the three groups and periods. Responses provided on a 100mm VAS.

Component	Baseline	6 mo.	12 mo.	GEE, P Value		
				Groups	Time	Interaction
General Satisfaction						
Nondiabetic	55 (46, 64)	85 (79, 91)	87 (81, 94)			
HbA1c < 8.1	54 (45, 64)	91 (86, 96)	88 (81, 94)	0.826$^{(ns)}$	<0.001*	0.136$^{(ns)}$
HbA1c ≥8.1	44 (32, 56)	95 (92, 97)	88 (79, 96)			

Table 4 Continued

Specific items						
Cleaning						
Nondiabetic	83 (76, 90)	93 (90, 96)	91 (86, 96)			
HbA1c < 8.1	85 (80, 91)	95 (94, 97)	95 (93, 97)	0.269(ns)	0.002*	0.874(ns)
HbA1c ≥8.1	86 (78, 94)	91 (86, 96)	89 (81, 97)			
Speech						
Nondiabetic	68(59, 78)	91 (88, 95)	89 (84, 94)			
HbA1c < 8.1	72 (63, 80)	94 (91, 97)	89 (83, 94)	0.832(ns)	<0.001*	0.701(ns)
HbA1c ≥8.1	73 (63, 82)	94 (89, 98)	85 (75, 96)			
Comfort						
Nondiabetic	53 (44, 63)	88 (82, 94)	84 (77, 91)			
HbA1c < 8.1	56 (47, 66)	90 (85, 96)	86 (79, 93)	0.804(ns)	<0.001*	0.510(ns)
HbA1c ≥8.1	46 (32, 59)	95 (92, 97)	89 (82, 95)			
Aesthetics						
Nondiabetic	77 (68, 85)	93 (91, 96)	92 (87, 96)			
HbA1c < 8.1	75 (68, 83)	96 (94, 98)	94 (91, 97)	0.521(ns)	<0.001*	0.438(ns)
HbA1c ≥8.1	65 (52, 78)	93 (86, 101)	96 (93, 99)			
Stability						
Nondiabetic	33 (24, 43)	83 (76, 89)	81 (73, 89)			
HbA1c < 8.1	42 (34, 51)	88 (81, 94)	85 (78, 91)	0.312(ns)	<0.001*	0.262(ns)
HbA1c ≥8.1	29 (17, 41)	89 (82, 95)	92 (84, 99)			

A first series of items dealing with chewing referred to the level of difficulty that participants rated their function (Table 5). The general item on chewing in general showed significant improvement from baseline to the six- (mean: 50 mm; 95% CI: 42 to 57 mm) and 12-month follow-up (mean: 46 mm; 95% CI: 37 to 55 mm). Differences between the six- and 12 month values were non-significant (mean: -4 mm; 95% CI: -10 to 2 mm). No difference was significant between groups, as well as the two-factor interaction.

All seven sub-items dealing with specific foods had similar results, i.e. difference from baseline to both follow-ups, with no difference between 6- and twelve-month results. Likewise, groups and interaction posed no significant effect.

Table 5. Mean values for the chewing ability-related items – chewing difficulties/"how difficult is to chew" (95% CI) according to the three groups and time periods. Responses provided on a 100mm VAS.

Component	Baseline	6 mo.	12 mo.	GEE, P Value		
				Groups	Time	Interaction
General ability						
Nondiabetic	38 (28, 48)	83 (77, 89)	84 (77, 91)			
HbA1c < 8.1	37 (28, 46)	87 (81, 94)	84 (77, 90)	0.925(ns)	<0.001*	0.532(ns)
HbA1c ≥8.1	35 (22, 47)	89 (83, 95)	80 (68,93)			
Specific foods						
White bread						
Nondiabetic	55 (45, 65)	87 (82, 92)	85 (78, 92)			
HbA1c < 8.1	53 (43, 63)	91 (86, 97)	82 (75, 89)	0.678(ns)	<0.001*	0.308(ns)
HbA1c ≥8.1	60 (46, 73)	87 (81, 94)	90 (83, 96)			
Hard cheese						
Nondiabetic	44 (34, 54)	83 (76, 90)	83 (77, 90)			
HbA1c < 8.1	44 (34, 53)	88 (81, 95)	84 (78, 91)	0.859(ns)	<0.001*	0.850(ns)
HbA1c ≥8.1	46 (32, 60)	84 (76, 92)	80 (68, 91)			
Raw carrots						
Nondiabetic	33 (24, 43)	83 (76, 89)	81 (73, 89)			
HbA1c < 8.1	42 (34, 51)	88 (81, 94)	85 (78, 91)	0.402(ns)	<0.001*	0.496(ns)
HbA1c ≥8.1	29 (17, 41)	89 (82, 95)	92 (84, 99)			
Salami						
Nondiabetic	39 (29, 49)	81 (74, 88)	81 (74, 88)			
HbA1c < 8.1	40 (30, 49)	74 (63, 85)	80 (71, 88)	0.491(ns)	<0.001*	0.869(ns)
HbA1c ≥8.1	45 (33, 57)	83 (73, 93)	84 (76, 92)			
Steak						
Nondiabetic	42 (33, 52)	82 (76, 88)	82 (76, 89)			
HbA1c < 8.1	37 (27, 46)	82 (75, 90)	81 (73, 89)	0.740(ns)	<0.001*	0.939(ns)
HbA1c ≥8.1	39 (25, 52)	79 (69, 90)	78 (67, 89)			

Table 5 Continued

Raw apples						
Nondiabetic	30 (21, 39)	69 (61, 78)	70 (60, 79)			
HbA1c < 8.1	25 (16, 34)	65 (55, 76)	69 (60, 79)	0.836$^{(ns)}$	<0.001*	0.133$^{(ns)}$
HbA1c ≥8.1	26 (16, 37)	76 (68, 85)	60 (44, 76)			
Lettuce						
Nondiabetic	52 (42, 61)	80 (74, 86)	83 (76, 90)			
HbA1c < 8.1	41 (31, 50)	77 (69, 86)	78 (71, 85)	0.243$^{(ns)}$	<0.001*	0.627$^{(ns)}$
HbA1c ≥8.1	50 (38, 63)	86 (79, 92)	82 (72, 91)			

*significant effect; $^{(ns)}$non-significant.

Chewing function, i.e. how well participants perceived food is chewed before swallowing, resulted in similar findings to the previous question subset (Table 6). Despite the non-significant effect of groups, time differences were significant when comparing baseline data with the 6-month and 12-month follow-up. In turn, both follow-up periods were not significantly different.

A single item of this subset resulted in significant interaction, namely the "chewing function - hard cheese" items. However, post-hoc tests showed results that are comparable to those for the other items, i.e. baseline results lower than follow-up; non-significant differences between 6 and 12 months, and non-significant differences between groups. Figure 4 further elucidates the interaction, which might have been caused by the larger differences between baseline and post-treatment values in diabetic participants compared to the control/nondiabetic group.

Table 6. Mean values for the chewing ability-related items – chewing function/"is food well chewed before swallowing?" (95% CI) according to the three groups and period. Responses provided on a 100mm VAS. Distinct uppercase letters represent significant between-group difference, whereas lowercase letters represent between-time differences ($P < .05$).

Component	Baseline	6 mo.	12 mo.	GEE, P Value		
				Groups	Time	Interaction
General function						
Nondiabetic	63 (54, 72)	83 (78, 89)	86 (80, 92)			
HbA1c < 8.1	54 (45, 63)	91 (87, 95)	85 (80, 90)	0.903$^{(ns)}$	<0.001*	0.028*
HbA1c ≥8.1	55 (43, 67)	88 (82, 94)	83 (73, 94)			
Specific foods						
White bread						
Nondiabetic	63 (54, 72)	84 (79, 90)	82 (74, 89)			
HbA1c < 8.1	57 (48, 67)	89 (83, 95)	84 (78, 90)	0.905$^{(ns)}$	<0.001*	0.534$^{(ns)}$
HbA1c ≥8.1	61 (50, 72)	86 (79, 93)	88 (83, 94)			
Hard cheese						
Nondiabetic	54 (44, 64)	79 (72, 87)	83 (76, 90)			
HbA1c < 8.1	46 (36, 56)	93 (88, 97)	83 (77, 90)	0.900$^{(ns)}$	<0.001*	0.023*
HbA1c ≥8.1	51 (37, 64)	88 (82, 95)	81 (71, 92)			
Raw carrots						
Nondiabetic	35 (24, 45)	72 (63, 80)	72 (62, 82)			
HbA1c < 8.1	27 (17, 36)	68 (56, 79)	70 (61, 80)	0.687$^{(ns)}$	<0.001*	0.369$^{(ns)}$
HbA1c ≥8.1	29 (15, 43)	76 (66, 86)	64 (49, 80)			
Salami						
Nondiabetic	45 (34, 55)	79 (71, 87)	80 (72, 88)			
HbA1c < 8.1	38 (27, 48)	81 (72, 90)	82 (75, 89)	0.519$^{(ns)}$	<0.001*	0.594$^{(ns)}$
HbA1c ≥8.1	52 (39, 66)	83 (73, 93)	82 (74, 91)			
Steak						
Nondiabetic	51 (41, 61)	82 (76, 88)	82 (75, 88)			
HbA1c < 8.1	42 (32, 52)	86 (79, 92)	81 (74, 88)	0.867$^{(ns)}$	<0.001*	0.507$^{(ns)}$
HbA1c ≥8.1	46 (32, 60)	83 (76, 91)	79 (67, 90)			
Raw apples						
Nondiabetic	43 (32, 54)	76 (68, 84)	75 (66, 84)			
HbA1c < 8.1	34 (24, 44)	78 (68, 87)	80 (73, 88)	0.984$^{(ns)}$	<0.001*	0.057$^{(ns)}$
HbA1c ≥8.1	38 (23, 54)	86 (80, 91)	71 (56, 85)			

Table 6 Continued

Lettuce						
Nondiabetic	55 (45, 64)	81 (74, 88)	82 (76, 89)			
HbA1c < 8.1	43 (33, 53)	81 (73, 89)	81 (75, 88)	0.193[ns]	<0.001*	0.589[ns]
HbA1c ≥8.1	53 (40, 66)	88 (83, 93)	87 (81, 93)			

*significant effect; [ns]non-significant.

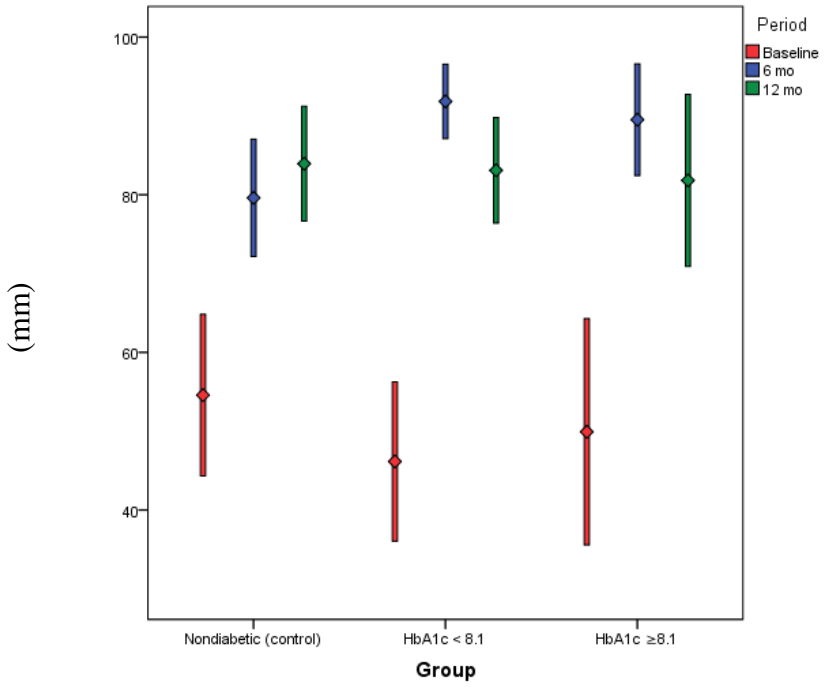

Figure 4. Chewing function with specific food – hard cheese before and following treatment, by group and timepoint. Diamonds represent mean values, whereas bars represent 95% CI.

Five-Group Analysis, Patient-Reported Outcomes

Further dividing participants into five groups resulted in similar results for the main patient-reported outcomes. Both general satisfaction and OHIP-EDENT – summary scores underwent significant effect of time (GEE, $p < 0.001$), with lower values on

baseline. Non-significant differences were found between 6- and 12-month results. Again, the effect of groups was not significant (satisfaction: p = 0.154; OHIP-EDENT; p= 0.530), as well as the two-factor interaction (satisfaction: p = 0.070; OHIP-EDENT; p = 0.433). Nevertheless, it is important to remark the sizeable 95% CI for groups "HbA1c < 6.1" and "HbA1c > 10.0" (Figure 5), justifying the use of the three-group division for more solid conclusions.

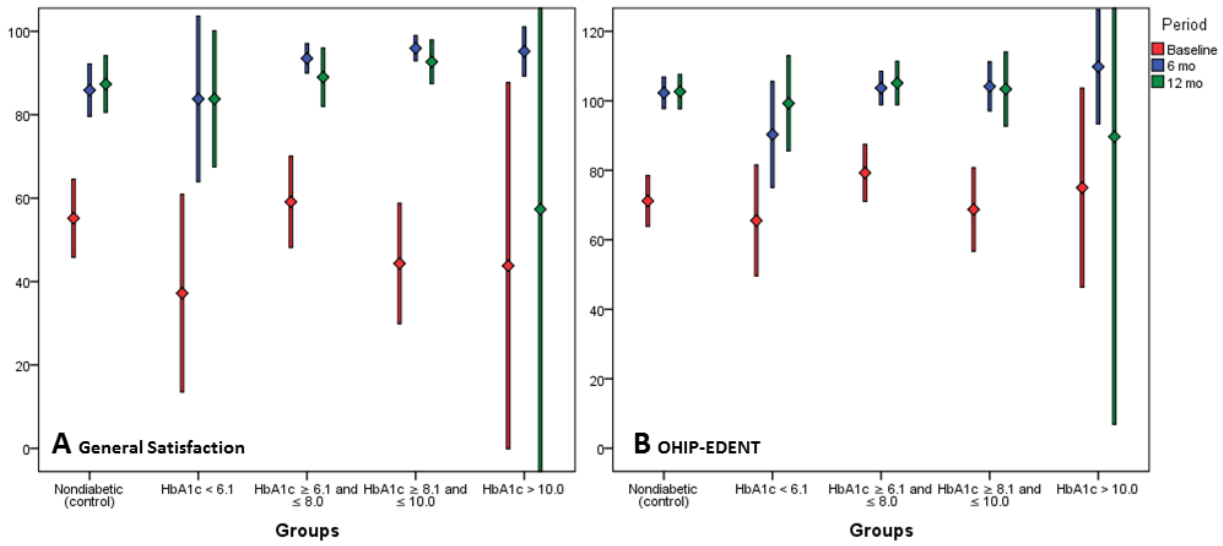

Figure 5. Mean values and 95% CI for (A) the general satisfaction (100-mm VAS), and (B) OHIP-EDENT, by five groups and periods.

HbA_{1c}

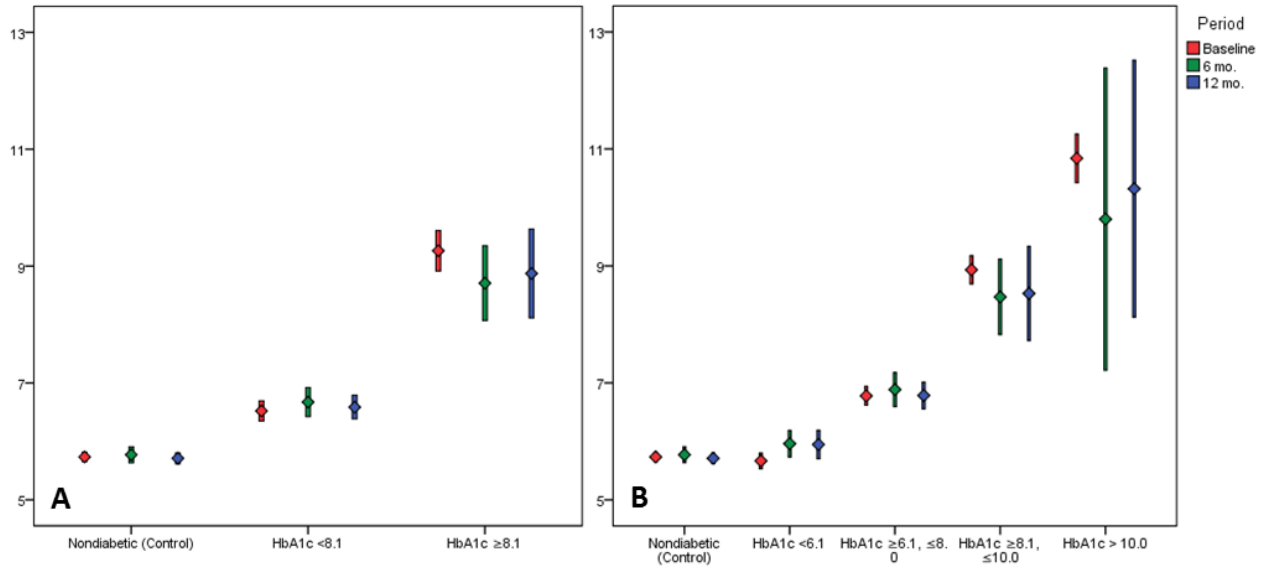

Figure 6. $HbA1_c$ before and following treatment, according to (A) the three-group, and (B) five-group divisions. Diamonds represent mean values, whereas bars represent 95% CI.

Table 7. Groups and period effects on $HbA1_c$, assessed by the GEE method.

Number of Groups	GEE, P Value		
	Differences between groups	Time	Interaction
Three	<0.001*	0.504$^{(ns)}$	0.193$^{(ns)}$
Five	<0.001*	0.682$^{(ns)}$	0.207$^{(ns)}$

*significant effect; $^{(ns)}$non-significant.

All between-group differences were significant for the three-group division (Bonferroni test, $p < 0.001$). Although $HbA1_c$ was not affected treatment over time, groups were significantly different. Such differences were stable during the study. $HbA1_c$ for both groups of diabetic patients was higher than for the non-diabetic group (well-controlled: 0.86, 95%CI: 0.58 to 1.12; poorly controlled: 3.19, 95%CI: 2.74 to 3.64). The difference between the two diabetic groups was 2.34, with 95%CI ranging from 1.88 to 2.80.

IV. Discussion

This prospective cohort study comparatively evaluated the effect of implant-supported restorations over 1 year on oral health quality of life (OHIP) and general satisfaction of edentulous patients with and without type 2 diabetes. The effect of implant-supported restoration on HbA1c levels over time was also evaluated.

Historically, diabetes has been identified as a relative risk factor for dental implants dependent on glycemic control. While there is emerging evidence that suggests diminished risks for implant complications associated with poor glycemic control, there is little evidence examining the potential for benefit of implant therapy in these patients (Oates et al., 2014). The goal of this investigation is to address this gap in information of patient related outcomes for consideration on the risk-benefit analysis to guide treatment decisions.

After tooth loss, patients avoid foods that are harder to masticate, possibly leading to nutritional compromise. Nutrition becomes even more important for diabetic patients critically dependent on dietary management. Furthermore, limiting the application of implant therapy to patients with good metabolic control may deprive those patients with poor metabolic control the opportunity to improve sufficiently to allow for the consideration of implant therapy. Therefore, these patients may remain unable to receive the benefits of implant therapy because of their poor control, and unable to improve their poor control because they have not been provided implant therapy.

The advantage of placing implants to support an overdenture and the improvement in quality of life and satisfaction has to be weighed against the risks of implant complications in uncontrolled diabetic patients. A recent systematic review

found no statistically significant difference between well-controlled type 2 diabetic subjects and non-diabetic patients for implant failure (Moraschini et al., 2016). Furthermore, the data from a single-center, prospective cohort study by Oates et al. (2014) demonstrated that elevated HbA1c levels in patients with type 2 diabetes were not associated with altered implant survival one year after loading. Importantly, this study evaluated patients with HbA1c levels approaching 12%. Additionally, this study showed that alterations in early bone healing and implant stability were associated with hyperglycemia.

Appropriate dental rehabilitation utilizing implant support has the potential to offer the patient with improved nutrition and metabolic control (Naujokat et al., 2016). The results of this 12-month study evaluating the benefits of implant mandibular overdentures shows that oral health quality of life was significantly better after the placement of implants to support their dentures. The magnitude of the benefit of implant-supported mandibular dentures is comparable to the impact found for healthy individuals (Emami et al., 2009; Kodama et al., 2016). Kapur et al. (1999) conducted a randomized trial to compare the efficacy of conventional mandibular and implant-supported overdentures in diabetic edentulous patients with clinically acceptable metabolic control. Longitudinal data for the satisfaction questionnaire showed improvements with both types of study dentures with higher improvements in the IOD than in the CD group.

Looking comparatively at patients based on diabetic status, there were no differences in benefit between groups. All groups regardless of metabolic control benefit from implant-supported overdentures compared with conventional dentures. A recent systematic review of the literature examining the efficacy of mandibular 2-implant

overdentures found that the difference in participant recruitment and their pretreatment condition were important sources of heterogeneity between studies (Kodama et al., 2016). This finding was in line with the Perneger conceptual model (Perneger, 2004) of patient satisfaction and supports the concept that pretreatment health status and the nature of the clinical problem should be considered when analyzing patient-based outcome. Nevertheless, implant overdentures (IOD) have a similar positive effect on patient's quality of life and satisfaction.

The OHIP-EDENT questionnaire was analyzed using the total score and seven subgroup domains, which include functional limitation, physical pain, psychological discomfort, physical disability, social disability and handicap. The comparison of pre- and post-treatment ratings showed that significant positive change (higher scores) had occurred in the total scores and on all domains following treatment. These findings are in accordance with recent systematic reviews in healthy individuals and controlled diabetics in improving patients' quality of life (Boven et al., 2015; Sivaramakrishnan et al., 2016).

The magnitude of the differences ranged considerably among different satisfaction items. Stability and comfort had drastic improvements compared to chewing function and other subsets of the 100mm VAS scale questions. Limitations of this study include the inability to analyze the changes in dietary intakes as measured by interviews, questionnaires and blood samples. Reviews on effects of overdentures have found that IOD do not seem to improve dietary intakes (Boven et al., 2015). These may be due to the fact that diet is a habit and behavioral interventions should be incorporated as part of a multidisciplinary approach to achieve lifestyle changes.

In analyzing the effects of IOD on glucose levels, it was found that HbA_{1c} was not affected by time. There is strong evidence that complex interventions, including dietary changes, can prevent the progression of impaired glucose tolerance to diabetes. A recent review by Zanuso et al. 2010 confirms the idea that diabetes therapy, including reduction in body fat and hyperglycemia, has been potentially reversible following appropriate lifestyle intervention that incorporates physical activity. Literature reviews (Ajala et al., 2013; Khazrai et al., 2014) have presented many dietary regimens available for patients with type 2 diabetes. Moreover, it is important to provide a tailor-made diet wherever possible in order to maximize the efficacy of the diet on reducing diabetes symptoms and encouraging patients' adherence.

The only intervention included in this study was that of dental implants on diabetic patients using complete dentures. Specific lifestyle interventions, such as diet modification, physical activity or exercise were not incorporated. Future research should involve the expertise of physicians, dentists, psychologists, nutritionist and physical trainers on the prevention and treatment of diabetes mellitus. This multidisciplinary approach could help individuals satisfactorily approach the complex challenge of living with a chronic disease.

In summary, diabetic patients benefit from implant-supported overdentures regardless of their glycemic control. Patient's quality of life, satisfaction, and function increase significantly when implants are used to support a mandibular overdenture. The improvement in chewing may be beneficial in a multidisciplinary intervention of glycemic control including diet, physical activity and habits.

V. Appendices

OHIP-20E Questionaire

Identification code : ☐☐☐☐☐☐☐☐☐☐

Date : ☐☐☐☐ / ☐☐ / ☐☐
a a m m j j

This questionnaire was designed to evaluate how your oral condition has affected your quality of life **during the past month**. For each of the following questions, mark the response that you feel is the best. If a question does not apply to your situation, then please indicate this just below the question.

	In the last month:	**Always**	**Most of the time**	**Some of the time**	**Occasionally**	**Rarely**	**Never**
1	Have you had difficulty chewing any foods because of problems with your teeth, mouth or dentures?	O 1	O 2	O 3	O 4	O 5	O 6
2	Have you had food catching in your teeth or dentures?	O 1	O 2	O 3	O 4	O 5	O 6
3	Have you felt that your dentures have not been fitting properly?	O 1	O 2	O 3	O 4	O 5	O 6
4	Have you had painful aching in your mouth?	O 1	O 2	O 3	O 4	O 5	O 6
5	Have you found it uncomfortable to eat any foods because of problems with your teeth, mouth or dentures?	O 1	O 2	O 3	O 4	O 5	O 6
6	Have you had sore spots in your mouth?	O 1	O 2	O 3	O 4	O 5	O 6
7	Have you had uncomfortable dentures?	O 1	O 2	O 3	O 4	O 5	O 6
8	Have you been worried by dental problems?	O 1	O 2	O 3	O 4	O 5	O 6
9	Have you been self conscious because of problems with your teeth, mouth or dentures?	O 1	O 2	O 3	O 4	O 5	O 6
10	Have you had to avoid eating some foods because of problems with your teeth, mouth or dentures?	O 1	O 2	O 3	O 4	O 5	O 6
11	Has your diet been unsatisfactory because of problems with your teeth, mouth or dentures?	O 1	O 2	O 3	O 4	O 5	O 6
12	Have you been unable to eat with your dentures because of problems with them?	O 1	O 2	O 3	O 4	O 5	O 6
13	Have you had to interrupt meals because of problems with your teeth, mouth or dentures?	O 1	O 2	O 3	O 4	O 5	O 6

	In the last month:	Always	Most of the time	Some of the time	Occasionally	Rarely	Never
14	Have you been upset because of problems with your teeth, mouth or dentures?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
15	Have you been a bit embarrassed because of problems with your teeth, mouth or dentures?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
16	Have you avoided going out because of problems with your teeth, mouth or dentures?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
17	Have you been less tolerant of your spouse or family because of problems with your teeth, mouth or dentures?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
18	Have you been a bit irritable with other people because of problems with your teeth, mouth or dentures?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
19	Have you been unable to enjoy other people's company as much because of problems with your teeth, mouth or dentures?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
20	Have you felt that life in general was less satisfying because of problems with your teeth, mouth or dentures?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6

ASSESSMENT OF PROSTHESIS

Last name : First name:

Date : / / (y y / m m / d d)

Baseline 3mo 6mo 12 mo 36mo 60mo

We would like to know how satisfied you are with your present prosthesis. Read each of the following questions and draw a vertical line on the horizontal line, where you think your answer best fits. In the case where a question doesn't apply to you, for example if you don't eat a certain type of food, write a brief explanation on the line.

1. Ease of cleaning

Please indicate how difficult it is to clean your **lower** prosthesis and mouth?

Extremely difficult _____ Not at all difficult ☐☐☐

2. General satisfaction

In general, are you satisfied with your **lower** prosthesis?

Not at all satisfied _____ Extremely satisfied ☐☐☐

3. Ability to speak

Please indicate how difficult it is for you to speak because of your lower prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

4. Comfort

Are you satisfied with the comfort of your **lower** prosthesis?

Not at all satisfied _____ Extremely satisfied ☐☐☐

5. Aesthetics

Are you satisfied with the appearance of your **lower** prosthesis?

Not at all satisfied _____ Extremely satisfied ☐☐☐

6. Stability

Are you satisfied with the stability of your **lower** prosthesis?

Not at all satisfied _____ Extremely satisfied ☐☐☐

7. Ability to chew

In general, do you find it difficult to chew food because of your **lower** prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

Please indicate how difficult it is for you to eat **fresh white bread** because of your **lower** prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

Please indicate how difficult it is for you to eat **hard cheese** because of your **lower** prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

Please indicate how difficult it is for you to eat **raw carrots** because of your **lower** prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

Please indicate how difficult it is for you to eat **dry salami** because of your **lower** prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

Please indicate how difficult it is for you to **sliced steak** because of your **lower** prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

Please indicate how difficult it is for you to eat **raw apples** because of your **lower** prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

Please indicate how difficult it is for you to eat **lettuce** because of your **lower** prosthesis?

Extremely difficult _____ Not at all difficult ☐☐☐

8. Function

In general, is your food well chewed before swallowing?

Badly chewed _____ Very well chewed ☐☐☐

Are pieces of **fresh white bread** well chewed before swallowing?

Badly chewed _____ Very well chewed ☐☐☐

Are pieces of **hard cheese** well chewed before swallowing?

Badly chewed _____ Very well chewed ☐☐☐

Are pieces of **raw carrot** well chewed before swallowing?

Badly chewed _____ Very well chewed ☐☐☐

Are pieces of **dry salami** well chewed before swallowing?

Badly chewed _____ Very well chewed ☐☐☐

Are pieces of **sliced steak** well chewed before swallowing?

Badly chewed _____ Very well chewed ☐☐☐

Are pieces of **raw apple** well chewed before swallowing?

Badly chewed _____ Very well chewed ☐☐☐

Are pieces of **lettuce** well chewed before swallowing?

Badly chewed _____ Very well chewed ☐☐☐

9. Oral condition

In general, are you satisfied with your oral condition?

Not at all satisfied _____ Extremely satisfied ☐☐☐

Do you believe that your oral condition has a negative effect on your general health? No ○$_0$ Yes ○$_1$ If yes, why? _____ _____ _____ _____ _____	☐

VI. References

Ajala, O., English, P., & Pinkney, J. (2013). Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes–. *The American journal of clinical nutrition*, *97*(3), 505-516.

Allen, F., & Locker, D. (2002). A modified short version of the oral health impact profile for assessing health-related quality of life in edentulous adults. *International Journal of Prosthodontics*, *15*(5).

Aoyama, N., Suzuki, J. I., Kobayashi, N., Hanatani, T., Ashigaki, N., Yoshida, A., ... & Isobe, M. (2017). Associations among tooth loss, systemic inflammation and antibody titers to periodontal pathogens in Japanese patients with cardiovascular disease. *Journal of periodontal research*.

Awad, M. A., Lund, J. P., Shapiro, S. H., Locker, D., Klemetti, E., Chehade, A., ... & Feine, J. S. (2003). Oral health status and treatment satisfaction with mandibular implant overdentures and conventional dentures: A randomized clinical trial in a senior population. *International Journal of Prosthodontics*, *16*(4).

Awad, M. A., Rashid, F., & Feine, J. S. (2014). The effect of mandibular 2-implant overdentures on oral health–related quality of life: an international multicentre study. *Clinical oral implants research*, *25*(1), 46-51.

Azogui-Lévy, S., Dray-Spira, R., Attal, S., Hartemann, A., Anagnostou, F., & Azerad, J. (2017). Factors associated with oral health-related quality of life in patients with diabetes. *Australian dental journal*.

Buckley, L. A., & Growley, M. J. (1984). A longitudinal study of untreated periodontal disease. *Journal of clinical periodontology*, *11*(8), 523-530.

Chapple, I. L., & Genco, R. (2013). Working group of joint EFP/AAP workshop. Diabetes and periodontal diseases: Consensus report of the joint EFP/AAP workshop on periodontitis and systemic diseases. Journal of Clinical Periodontology, 40(14), S106–S112.

Chrcanovic, B. R., Albrektsson, T., & Wennerberg, A. (2014). Diabetes and oral implant failure: a systematic review. *Journal of Dental Research*, *93*(9), 859-867.

Diabetes Control and Complications Trial Research Group. (1993). The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *New England journal of medicine*, *329*(14), 977-986.

Dowell, S., Oates, T. W., & Robinson, M. (2007). Implant success in people with type 2 diabetes mellitus with varying glycemic control: a pilot study. *The Journal of the American Dental Association*, *138*(3), 355-361.

Feine, J. S., Carlsson, G. E., Awad, M. A., Chehade, A., Duncan, W. J., Gizani, S., ... & Mojon, P. (2002). The McGill consensus statement on overdentures. Mandibular two-implant overdentures as first choice standard of care for edentulous patients. Montreal, Quebec, May 24-25, 2002. *The International journal of oral & maxillofacial implants*, *17*(4), 601.

Fiorellini, J. P., Chen, P. K., Nevins, M., & Nevins, M. L. (2000). A retrospective study of dental implants in diabetic patients. *International Journal of Periodontics & Restorative Dentistry*, *20*(4).

Fiorellini, J. P., Nevins, M. L., Norkin, A., Weber, H. P., & Karimbux, N. Y. (1999). The effect of insulin therapy on osseointegration in a diabetic rat model. *Clinical oral implants research*, *10*(5), 362-368.

Gerritsen, M., Lutterman, J. A., & Jansen, J. A. (2000). Wound healing around bone-anchored percutaneous devices in experimental diabetes mellitus. *Journal of Biomedical Materials Research Part A*, *53*(6), 702-709.

Hajishengallis, G., & Lamont, R. J. (2012). Beyond the red complex and into more complexity: the polymicrobial synergy and dysbiosis (PSD) model of periodontal disease etiology. *Molecular oral microbiology*, *27*(6), 409-419.

Kapur, K. K., Garrett, N. R., Hamada, M. O., Roumanas, E. D., Freymiller, E., Han, T., ... & Ida, R. (1998). A randomized clinical trial comparing the efficacy of mandibular implant-supported overdentures and conventional dentures in diabetic patients. Part I: Methodology and clinical outcomes. *Journal of Prosthetic Dentistry*, *79*(5), 555-569.

Kassebaum, N. J., Bernabé, E., Dahiya, M., Bhandari, B., Murray, C. J. L., & Marcenes, W. (2014). Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. *Journal of dental research*, *93*(11), 1045-1053.

Kawamura, M., Tsurumoto, A., Fukuda, S., & Sasahara, H. (2001). Health behaviors and their relation to metabolic control and periodontal status in type 2 diabetic patients: a model tested using a linear structural relations program. *Journal of periodontology*, *72*(9), 1246-1253.

Khandelwal, N., Oates, T. W., Vargas, A., Alexander, P. P., Schoolfield, J. D., & Alex McMahan, C. (2013). Conventional SLA and chemically modified SLA implants in patients with poorly controlled type 2 diabetes mellitus–a randomized controlled trial. *Clinical oral implants research*, *24*(1), 13-19.

Khazrai, Y. M., Defeudis, G., & Pozzilli, P. (2014). Effect of diet on type 2 diabetes mellitus: a review. *Diabetes/metabolism research and reviews*, *30*(S1), 24-33.

Knight 2016. Risk factors that may modify the innate and adaptive immune responses in periodontal diseases. Kodama, N., Singh, B. P., Cerutti-Kopplin, D., Feine, J., & Emami, E. (2016). Efficacy of Mandibular 2-implant Overdenture: An Updated Meta-analysis on Patient-based Outcomes. *JDR Clinical & Translational Research*, *1*(1), 20-

30.

Lawal, F. B., Taiwo, J. O., & Arowojolu, M. O. (2014). How valid are the psychometric properties of the oral health impact profile-14 measure in adult dental patients in Ibadan, Nigeria?. *Ethiopian journal of health sciences*, *24*(3), 235-242.

Locker, D. (1988). Measuring oral health: a conceptual framework. *Community Dent Health*, *5*, 3-18.

Löe, H., Anerud, A., Boysen, H. and Morrison, E. (1986), Natural history of periodontal disease in man. Journal of Clinical Periodontology, 13: 431–440. doi:10.1111/j.1600-051X.1986.tb01487.x

Mealey, B. L., & Oates, T. W. (2006). Diabetes mellitus and periodontal diseases. *Journal of periodontology*, *77*(8), 1289-1303.

Monje, A., Catena, A., & Borgnakke, W. S. (2017). Association between Diabetes Mellitus/Hyperglycemia and Peri-Implant Diseases: Systematic Review and Meta-Analysis. *Journal of clinical periodontology*.

Moraschini, V., Barboza, E. S. P., & Peixoto, G. A. (2016). The impact of diabetes on dental implant failure: a systematic review and meta-analysis. *International journal of oral and maxillofacial surgery*, *45*(10), 1237-1245.

Naujokat, H., Kunzendorf, B., & Wiltfang, J. (2016). Dental implants and diabetes mellitus—a systematic review. *International journal of implant dentistry*, *2*(1), 5.

Nevins, M. L., Karimbux, N. Y., Weber, H. P., Giannobile, W. V., & Fiorellini, J. P. (1998). Wound healing around endosseous implants in experimental diabetes. *International Journal of Oral & Maxillofacial Implants*, *13*(5).

Nield, L., Moore, H., Hooper, L., Cruickshank, K., Vyas, A., Whittaker, V., & Summerbell, C. D. (2007). Dietary advice for treatment of type 2 diabetes mellitus in adults. *The Cochrane Library*.

Nuttall, F. Q., Gannon, M. C., Saeed, A., Jordan, K., & Hoover, H. (2003). The metabolic response of subjects with type 2 diabetes to a high-protein, weight-maintenance diet. *The Journal of Clinical Endocrinology & Metabolism*, *88*(8), 3577-3583.

Oates, T. W., Dowell, S., Robinson, M., & McMahan, C. A. (2009). Glycemic control and implant stabilization in type 2 diabetes mellitus. *Journal of dental research*, *88*(4), 367-371.

Oates, T. W., Galloway, P., Alexander, P., Green, A. V., Huynh-Ba, G., Feine, J., & McMahan, C. A. (2014). The effects of elevated hemoglobin A1c in patients with type 2 diabetes mellitus on dental implants. *The Journal of the American Dental Association*, *145*(12), 1218-1226.

Oates, T. W., Huynh-Ba, G., Vargas, A., Alexander, P., & Feine, J. (2013). A critical review of diabetes, glycemic control, and dental implant therapy. *Clinical oral implants research*, *24*(2), 117-127.

Patel, M. H., Kumar, J. V., & Moss, M. E. (2013). Diabetes and tooth loss: an analysis of data from the National Health and Nutrition Examination Survey, 2003–2004. *The Journal of the American Dental Association*, *144*(5), 478-485.

Perneger, T. V. (2004). Adjustment for patient characteristics in satisfaction surveys.

Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010: 87: 4–14

Sheiham, A., Steele, J. G., Marcenes, W., Lowe, C., Finch, S., Bates, C. J., ... & Walls, A. W. G. (2001). The relationship among dental status, nutrient intake, and nutritional status in older people. *Journal of dental research*, *80*(2), 408-413.

Sivaramakrishnan, G., & Sridharan, K. (2016). Comparison of implant supported mandibular overdentures and conventional dentures on quality of life: a systematic review and meta-analysis of randomized controlled studies. *Australian dental journal*, *61*(4), 482-488.

Slade, G. D. (Ed.). (1997). *Measuring oral health and quality of life*. Department of Dental Ecology, School of Dentistry, University of North Carolina.

Slade, G. D., & Spencer, A. J. (1994). Development and evaluation of the oral health impact profile. *Community dental health*, *11*(1), 3-11.

Swati, S. (2013). Implants in Diabetic Patients. *Int J Oral Implantol*, *4*(1), 30-35.

Thomason, J. M., Kelly, S. A. M., Bendkowski, A., & Ellis, J. S. (2012). Two implant retained overdentures—A review of the literature supporting the McGill and York consensus statements. *Journal of dentistry*, *40*(1), 22-34.

UK Prospective Diabetes Study (UKPDS) Group. (1998). Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *The Lancet*, *352*(9131), 854-865.

World Health Organization (2011) Fact Sheet No. 312. Diabetes [WWW document]. Available at: http://www.who.int/mediacentre/factsheets/ fs312/en/ [accessed on 23 August 2012].

Xiao, E., Mattos, M., Vieira, G. H. A., Chen, S., Corrêa, J. D., Wu, Y., ... & Graves, D. T. (2017). Diabetes enhances IL-17 expression and alters the oral microbiome to increase its pathogenicity. *Cell host & microbe*, *22*(1), 120-128.

Zanuso, S., Jimenez, A., Pugliese, G., Corigliano, G., & Balducci, S. (2010). Exercise for the management of type 2 diabetes: a review of the evidence. *Acta diabetologica*, *47*(1), 15-22.