Received: 26 October 2018 | Revised: 8 March 2019 | Accepted: 12 March 2019

DOI: 10.1111/cid.12769

WILEY

ORIGINAL ARTICLE

The All-on-4 treatment concept for the rehabilitation of the completely edentulous mandible: A longitudinal study with 10 to 18 years of follow-up

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Funding information
Nobel Biocare Services AG, Grant/Award Number: 2017-1534

Abstract

Background: There is a need for studies evaluating the long term outcomes of the All-on-4 treatment concept.

Purpose: To evaluate the long term clinical and radiographic outcomes of the All-on-4 treatment concept in the mandible.

Materials and Methods: This retrospective longitudinal case series study included 471 patients (women: 286, men: 185, average age = 57.7 years) rehabilitated with 1884 implants in immediate function supporting 471 fixed full-arch mandibular prostheses and followed for 10 to 18 years. Primary outcome measures were prosthetic survival and implant success and survival (estimated using life tables). Secondary outcome measures were marginal bone loss (MBL) at 10 and 15 years, biological and mechanical complications. Multivariable analysis was used to estimate potential risk indicators for implant failure (Cox regression to estimate hazard ratios and 95% confidence intervals (95%CI)), MBL > 3 mm at 10 and 15 years, biological and mechanical complications (binary logistic regression to estimate odds ratios [ORs] with 95%CI).

Results: Twenty-seven patients deceased (5.7%) and 149 patients (31.6%) were lost to follow-up. The cumulative prosthetic survival rate was 98.8%; the implant cumulative survival and success rate was 93% and 91.7%, respectively up to 18 years of follow-up. Previous biological complications (HR = 4.43) were significantly associated with implant failure. Average (95% CI) MBL at 10- and 15-years were 1.72 mm (95%CI: 1.59, 1.85) and 2.32 mm (95% CI: 1.98, 2.66). Smoking (OR = 2.72), previous failure of a contiguous implant (OR = 3.89) and biological complication (OR = 8.11) were associated with MBL > 3 mm. The incidence of biological complications was 11.8% at implant level, with previous failure of a contiguous implant (OR = 5.56), smoking (OR = 1.75), and systemic condition (OR = 1.65) were significantly associated. The incidence of mechanical complications was 36.7% with male gender (OR = 1.67) and type of prosthetic material used in the restoration significantly associated (metal-acrylic OR = 0.30; metal-ceramic OR = 0.22)).

Conclusions: Considering the implant, prosthetic and MBL outcomes it is concluded that the All-on-4 is a viable treatment option validated in the long term. Nevertheless, biological and mechanical complications can occur.

KEYWORDS

All-on-4, complete edentulous, dental implants, immediate function, long term, mandible

1 | INTRODUCTION

Over 275 million people are globally affected by severe tooth loss, with a 27% increase in the prevalence in the last decade between 2005 and 2015.[1]

Even though various treatment approaches are available for the restoration of partially edentulous patients, the restoration of fully edentulous jaws has been revolutionized, thanks to the introduction of implant-supported restorations.[2]

The use of osseointegrated dental implants in clinical practice began more than five decades ago with the novel work of Brånemark.[3] Giving the combination of factors: age-related tooth loss, anatomical condition of edentulous ridges, decreased performance of removable prosthesis, and predictable long-term results of implant therapy, demand for implant treatment is increasing,[4] specifically immediate function/loading protocols[5] Immediate loading of all-acrylic, implant-supported prostheses for maxillary and mandibular arches has been shown to provide advantages to patients (psychological and economic benefits)[6,7] and dentists (clinical and economic benefits)[7,8] with its predictability[9] associated with a high level of patient satisfaction.[2]

The rehabilitation of severely atrophic mandible using implant-supported prosthesis is often challenging because of the poor quality and quantity of residual jawbone posterior to the inferior alveolar nerve, especially in patients with long-term edentulism. Furthermore, progressive bone loss in the posterior mandible may lead to a superficialization of the alveolar nerve, which may cause pain to denture wearers during function.[4] At the beginning of the millennium, distally tilted implants were proposed for these situations, providing a significant alternative for the maxillary and mandibular posterior segments without bone grafting, with posterior tilting of distal implants enabling the use of denser bone located in the anterior aspects of maxilla and mandible, reduce cantilever lengths, broaden the prosthetic base, and improve implant-to-bone surface areas because longer implants can be used.[6,10] The optimal number of four implants in edentulous jaws was previously reported in the literature with favorable 5 to 10 years results.[11–13] The use of tilted implants together with the optimal number of four implants to rehabilitate the completely edentulous mandible with a full-arch fixed prosthesis was further adjusted by using immediate-function protocols with the connection of the prosthesis on the day of surgery (the All-on-4 concept is one of such concepts).[6] The development to fewer implants (n = 4) was justified provided they were placed as "cornerstones": two posterior implants tilted distally and two anterior implants placed in an axial position, all well spread; which with optimal implant anchorage could render a high probability for success.[6]

The All-on-4 treatment concept demonstrated to be a predictable treatment modality for full-arch rehabilitation with good results in the short-, medium- and long-term outcomes (up to 10 years).[6,14,15] An important aspect in the evaluation of implant-supported restorations concerns the evaluation not only of implant survival and success rates, but also the occurrence of biological and technical complications. Despite the occurrence of biological and technical complications, the same were considered minor and resolved chairside as previously reported in a follow-up up to 7 years.[16] However, evidence is lacking in the literature for outcomes exceeding 10 years in full-arch rehabilitation through this treatment modality using larger samples. The aim of this study is to report the long-term outcomes of full-arch mandibular rehabilitations through the All-on-4 concept (with Malo Clinic Protocol).

2 | MATERIALS AND METHODS

This article was written following the STROBE guidelines for observational studies.[17] This retrospective case series study included patients treated at a private rehabilitation center (Maló Clinic, Lisbon, Portugal) and it was approved by an independent ethics committee (Ethical Committee for Health, Lisbon, Portugal; Authorization n°04/2017). A chart review of patients rehabilitated with All-on-4 concept in the mandible was performed. The All-on-4 treatment concept consists in a full-arch implant-supported rehabilitation for complete edentulous jaws dependent of the position and anatomy of the mental nerve. Considering the guideline, the following decision tree was applied as inclusion criteria for the rehabilitation through the All-on-4 treatment concept: patients in need of a full-arch restoration through immediate function in the presence of a complete edentulous mandible with a residual bone height and width that enabled the insertion of implants with at least 7 mm of length and 3.75 mm of diameter; in the presence of periodontally or hopeless teeth that needed to be extracted while assuring the minimum bone height/width conditions for implant insertion after performing bone regularization; in the presence of potentially viable teeth in the anterior segment and absence of teeth in the posterior segments forcing bone grafting or nerve transposition before inserting dental implants, teeth were extracted and the All-on-4 treatment concept was applied aiming for a reduction in morbidity, treatment time, complexity and financial cost for the patient. The exclusion criteria for treating a patient were active chemotherapy or radiotherapy, enough bone height/width in the posterior segments to insert dental implants for partial restoration, the presence of healthy teeth in the posterior segments; patients who did not complete the rehabilitation protocol at the rehabilitation center (being referred exclusively for the implant insertion with or without a provisional restoration: n = 183 patients). Inclusion criterion to be selected for the study were patients with full-arch rehabilitation in the mandible through the All-on-4 concept that completed the rehabilitation protocol at the rehabilitation center. A total of 654 patients were treated in the mandible according to the All-on-4 concept. Patients were treated between April 1998 and December 2006:324 patients from an initial cohort[12] and 147 patients included between February and December of 2006; routine follow-up was performed between April 1998 and December 2016; data collection and analysis was performed between January and June 2018.

2.1 | Surgical protocol

The medical history of each patient was reviewed and the diseases were coded using the International Classification of Diseases, version 11 (ICD-11).[18] Each patient received a clinical examination and complementary

radiographic examinations, with an orthopantomography to assess bone height and computerized tomography scan to assess bone volume and anatomical structures such as the dental nerve. The surgical procedures were described in previous reports of the All-on-4 treatment concept surgical protocol.[6,14,15] In brief, insertion of the implants used in this study (Brånemark System Mk II, Mk III, Mk IV, and NobelSpeedy; Nobel Biocare AB, Göteborg, Sweden) followed standard procedures. The implant site preparation was performed according to the bone density in order to achieve the necessary primary stability (aiming to achieve a final torque >30 Ncm and maximum of 50 Ncm). For low density bone only the first drill (2 mm twist drill; Nobel Biocare AB) was used the full length of the implant site; for medium bone density the 2 mm and the 2.8 mm twist drills were used full length of the implant site (or later the twist step drill 2.4/2.8 mm; Nobel Biocare AB); while for dense bone all three drills were used (2 mm, 2.4/2.8 mm and 3.2/3.6 mm; Nobel Biocare AB). The length of the implants (all anterior to the foramina) ranged from 8.5 to 18 mm. The two most anterior implants followed jaw anatomy in direction (lingual tilting in cases of severe mandibular resorption). The two posterior implants were inserted just anterior to the foramina and tilted distally ~45° relative to the occlusal plane, aiming for good implant anchorage, short cantilever length, and large interimplant distance[14,15] as the posterior implants typically emerged at the second premolar position. The implant platform was positioned 0.8 mm above the bone crest for MkII, MkIII, and MkIV implants (corresponding to the lower corner of the cylindrical part of the implant flange was placed flush to bone crest) or flush to the bone crest for NobelSpeedy implants. The soft tissues were readapted and sutured back into position with 4-0 nonresorbable silk sutures (B Braun Silkam, Aesculap Inc, Center Valley, Pennsylvania). Estheticone abutments (Nobel Biocare AB) were used between April 1998 and June 2002. Straight or 17° angulated multiunit abutments (Nobel Biocare AB) were placed for anterior implants, and angulated 30° multiunit abutments (Nobel Biocare AB) were placed for posterior implants. The abutment angulations were chosen so that the prosthetic screw access holes were in occlusal or lingual locations, to keep the prosthesis with an acceptable thickness and to allow the prosthesis to have passive fit (the connection of the prosthesis without placing any stress on the supporting implants as evaluated by the one-screw test and clinical/radiographic analysis).

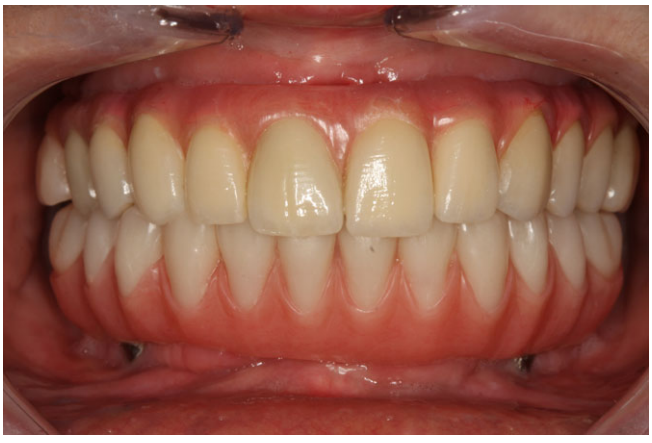

FIGURE 1 Representative intraoral photograph of a patient rehabilitated with a mandibular All-on-4 currently with 18 years of follow-up

2.2 | Immediate provisional prosthetic protocol

Implant-supported fixed prostheses of high-density acrylic resin (PalaXpress Ultra; Heraeus Kulzer GmbH, Germany) with titanium cylinders (Nobel Biocare AB) were manufactured at the dental laboratory and inserted on the same day. Anterior occlusal contacts and canine guidance during lateral movements were preferred in the provisional prosthesis. No cantilevers were used in the provisional bridges. Emergence positions of the screw-access holes at the posterior implants of the prostheses were normally at the level of the second premolar. Posterior tilting of the distal implants allowed the prostheses to hold a minimum of 10 teeth.

2.3 | Final prosthetic protocol

Considering the patients' financial capability, the provisional prosthesis was replaced by a metal ceramic implant-supported fixed prosthesis with a titanium framework and all-ceramic crowns (Procera titanium framework, Procera Alumina crowns, NobelRondo ceramics; Nobel Biocare AB), a metal-acrylic resin implant-supported fixed prosthesis with a titanium framework (Procera titanium framework; Nobel Biocare AB) and acrylic resin prosthetic teeth (Heraeus Kulzer GmbH), or a high-density acrylic resin (PalaXpress Ultra; Heraeus Kulzer GmbH, Germany) with titanium cylinders (Nobel Biocare AB). In this final prosthesis, the occlusion mimicked natural dentition. The final prosthesis was typically delivered 6 months after the surgery. A clinical long-term example is illustrated in Figures 1–3.

2.4 | Follow-up visits and maintenance protocol

The patients were instructed for soft food diet in the first months. A postoperative maintenance protocol was indicated to each patient including oral hygiene instructions.[19] Follow-up clinical appointments were performed at 10 days, 2, 4, and 6 months, 1 year and every 6 months thereafter, consisting in the assessment of clinical parameters, prophylaxis and dental hygiene instructions.

2.5 | Outcome measures

Primary outcome measures were prosthetic survival and implant success. Prosthetic survival was based on function, with the necessity of

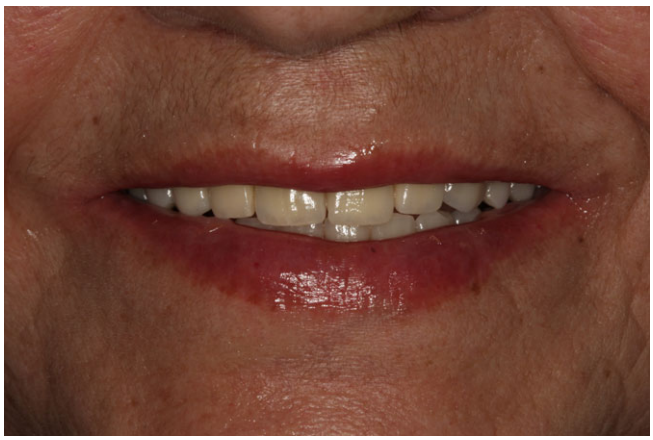

FIGURE 2 Representative extra-oral photograph of the same patient as in Figure 1 with the patient smiling

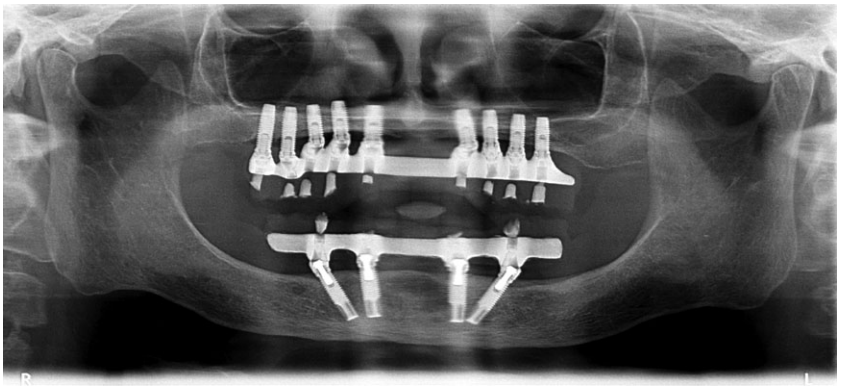

FIGURE 3 Representative orthopantomography of the same patient as in Figures 1 and 2, currently with 18 years of follow-up

replacing the prosthesis classified as failure. Implant success was based on the Maló Clinic success criteria:[20] (a) implant fulfilled its purported function as support for reconstruction (the potential existence of a sleeping implant was considered a failure); (b) implant was stable when individually and manually tested; (c) no signs of persistent infection that could jeopardize the implant outcome; (d) no radiolucent areas around the implants; (e) good esthetic outcome in the rehabilitation (classified as the absence of esthetic complains from the patient or Prosthodontist); and (f) allowed construction of an implant-supported fixed prosthesis, which provided patient comfort and good hygienic maintenance (classified as the absence of comfort and hygiene complains from the patient). Implants not complying with the criteria were considered survivals. Implant removal was classified as failure.

The secondary outcome measures were marginal bone loss (MBL) at the 10- and 15-years follow-up and the incidence of biological and mechanical complications. Periapical radiographs were taken on the day of surgery, 10- and 15-years using the parallel technique with a film holder (Super-Bite, Hawe Neos Dental, Bioggio, Switzerland), and its position was adjusted manually for an estimated orthogonal film position. An operator blinded to patient information examined radiographs of the implants to determine marginal bone level at each evaluation point. Each periapical radiograph was scanned at 300 dpi (HP Scanjet 4890; HP Portugal, Paço de Arcos, Portugal), and marginal bone level was assessed with image analysis software (Image J version 1.40 g for Windows, National Institutes of Health, Bethesda, Maryland). The reference point for the reading was the implant platform (horizontal interface for the axial implants and the orthogonal interface for tilted implants between implant and abutment), and marginal bone level was measured from this reference point to the first contact between implant and bone. The measurements were performed on the mesial and distal sites, and average values were calculated. The marginal bone level at 10- and 15-years were compared with the measurement at the day of surgery and MBL was calculated. The radiographs were accepted or rejected for evaluation based on the clarity of the implant threads: a clear thread guarantees both sharpness and an orthogonal direction of the radiographic beam towards the implant axis. The radiographs were calibrated using the implants' interthread length.

Biological complications concerning abscess, fistulae formation and peri-implant disease (the presence of peri-implant pockets ≥5 mm, bleeding on probing, with concurrent presence of MBL and clinical attachment loss) performed using a plastic periodontal probe calibrated to 0.25 N (Hawe Click Probe, Hawe Neos, Bioggio, Switzerland); and mechanical complications concerning loosening or fracture of any prosthetic component were assessed throughout the study follow-up and registered as present or absent.

2.6 | Statistical analysis

Descriptive statistics were computed for prosthetic survival (using the prosthesis as unit of analysis), implant survival and success (using the implants as unit of analysis), and MBL (using the implant as unit of analysis). The cumulative prosthesis survival, cumulative implant success, and cumulative implant survival were estimated through life tables. The Cox proportional hazards regression model was used to evaluate possible predictors of implant failure at 10 years using the patient as unit of analysis (patients presenting at least one implant failure compared to patients without any implant failures). The hazard is a measure of risk where the hazard function gives the instantaneous potential per unit time for the event to occur, providing an insight into the conditional failure rates, being the vehicle by which mathematical modeling of survival data is used in order to identify a specific model form.

Considering the statistical assumptions of this method, right censoring was applied at 10 years of follow-up and the failures occurring after 10th year of follow-up were not accounted in the multivariable analysis. We used univariable analyses to identify covariates associated with implant failure: age, gender, systemic condition (absence/presence), smoking status (smoker/nonsmoker), type of opposing dentition (implant-supported fixed prosthesis, natural tooth-supported fixed prosthesis, natural teeth, miscellaneous, removable denture), type of prosthetic material used in the restoration (metal-ceramic, metal-acrylic, acrylic resin), cantilever size (no cantilever, one unit cantilever, two units cantilever), mechanical complications (presence/absence), biological complications (presence/absence). Covariates ($P < 0.20$ in univariable analyses) and biologically relevant variables were then entered into a multivariable Cox proportional hazards regression model; regression coefficients were estimated with corresponding SEs.[21]

For the outcome variables “marginal bone loss >3 mm” (the presence of at least one implant with this criteria), “biological

complications" (the presence of at least one implant with this criteria) and "mechanical complications" a binary logistic regression model was computed to estimate the odds ratios (ORs) and corresponding 95% confidence intervals (CIs) for the explanatory variables using the patient as unit of analysis. The OR represents a measure of association between exposure and outcome, representing the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of exposure. We used univariable analyses to identify covariates associated with the outcome variables (all covariates described in the Cox regression analysis together with the variable "previous failure of a contiguous implant within the rehabilitation"). Covariates potentially significant ($P < 0.20$ in univariable analyses) were entered into a multivariable logistic regression model. The level of significance was 0.05. Statistics were computed using SPSS 17.0 (IBM, Rochester, New York).

3 | RESULTS

3.1 | Patient characteristics and drop-out rate

Between April 1998 and December 2006, 471 patients (286 women and 185 men; average age = 57.7 years old, range: 20-85 years old) received a full-arch rehabilitation in the mandible supported by four immediately loaded dental implants placed anterior to the mental foramina, in a total of 1884 implants (n = 219 machined surface implants inserted from April 1998; n = 1665 anodically oxidized surface implants-TiUnite, Nobel Biocare; inserted since April 2001; Table 1). A total of 224 patients were positive for ICD-11 with 117 patients who were smokers (24.8%) and 133 patients (28.2%) who had one systemic condition (Table 2). Regarding opposing dentition, 210 patients had an implant-supported fixed prosthesis, 54 patients had natural teeth, 28 patients had fixed prosthetics over natural teeth, 68 patients had a combination of natural teeth and implant-supported fixed prosthetics (miscellaneous), and 111 patients had a removable prosthesis.

A total of 166 patients was lost to follow-up (with 27 patients deceased due to causes unrelated to the implant treatment and 149 patients missing the control appointments) with the distribution according to follow-up time illustrated in Table 2.

TABLE 1 Implant distribution by design

Type of implant	Total number of implants (implant failures)
Brånemark System Mk II implants	42 (5)
Brånemark System Mk III implants	657 (25)
Machined surface	167 (8)
TiUnite surface	488 (17)
Brånemark System Mk IV implants	416 (14)
Machined surface	12 (0)
TiUnite surface	404 (14)
NobelSpeedy Groovy	769 (26)
Total	1884 (70)

3.2 | Prosthetic survival and implant success

Four prostheses were lost after 22, 113, 127, and 149 months in four patients who lost all four implants, rendering a 98.8% cumulative prosthetic survival rate.

Considering the evaluation of the implants success criteria, a total of 70 implants were removed and failed in 41 patients (8.7% failure rate at patient level), rendering a cumulative implant survival rate of 96.9% at 10 years and 93% up to 18 years of follow-up (life table analysis, Table 3); In addition, 19 implants in 19 patients were classified as survivals due to presenting signs of persistent infection that could jeopardize the implant outcome with MBL extending beyond 50% of the implants' length, rendering a cumulative implant success rate of 95.9% at 10 years and 91.7% up to 18 years of follow-up (life table analysis, Table 4; Figure 4). The distribution of survival according to the health status of the patients (healthy or systemic compromised/smoker) is illustrated in Figure 5. The remaining 37 patients with implant failures but without prosthetic failure maintained the prosthesis in function through reimplantation of maintaining the prosthesis supported on the remaining implants. The insertion of new implants with immediate loading for complementing the prosthetic support occurred immediately on the day of failure (n = 7 patients) or 4 to 6 months after implant failure (n = 20 patients) and was successful in all patients, nevertheless one patient that lost implants a second time and new implants were inserted a second time. The new implants were not accounted in the analysis for this study. During the healing time between implant failure and implant insertion, the prosthesis remained in function supported by the remaining implants, while after the healing time, the prosthesis was adapted to the new implant position. In 10 patients that refused further surgery, no implants were inserted and the prosthesis remained in function supported on three implants (n = 9 patients) and two implants (n = 1 patient) during the remaining follow-up of the study.

3.3 | Cox proportional hazards regression analysis of implant failure

Implant failure in the first decade of follow-up occurred in 36 patients. The Cox proportional hazards regression model was used to evaluate the relationship between implant failure and potential risk indicators with biological complications (HR = 4.62) significantly associated with implant failure after controlling for the presence of age, gender, smoking, and cantilever size (Table 5).

3.4 | Marginal bone loss

At the 10-year follow-up, 281 of the 320 patients had readable radiographs (87.8%). The average marginal bone level below the implant-abutment interface at baseline was −0.02 mm for NobelSpeedy implants and −0.82 mm for MkII, MkIII, and MkIV implants. The average (95% confidence interval) MBL was 1.7 mm (95% CI: 1.6, 1.9; range: 0.7-4.4) (Figure 6). At the 15-year follow-up, all 21 patients had readable radiographs (100%). The average MBL was 2.3 mm (95% CI: 2.0, 2.7; range: 1.1-6.0) (Figure 6).

TABLE 2 Overall medical status distribution according to the International Classification of Disease, version 11 (ICD-11); Distribution of patients deceased and lost to follow-up in the sample

ICD-11 classification	ICD-11 group description	Examples	Number of patients	Number of implants
1	Certain infectious or parasitic diseases	(HIV, hepatitis)	11	44
2	Neoplasms	(Cancer)	4	16
3	Diseases of the blood or blood forming organs	(Coagulation problems)	1	4
5	Endocrine, nutritional of metabolic diseases	(Diabetes, Hypercholesterolemia, Hyperthyroidism)	17	68
6	Mental, behavioral or neurodevelopmental disorders	(Anxiety)	3	12
8	Diseases of the nervous system	(Alzheimer, Epilepsy)	6	24
11	Diseases of the circulatory system	(Hypertension, Arrhythmia, Angina)	77	308
12	Diseases of the respiratory system	(Emphysema)	3	12
13	Diseases of the digestive system	(Heavy bruxer)	5	20
14	Diseases of the skin	(Epidermolysis bullosa)	1	4
15	Diseases of the musculoskeletal system or connective tissue	(Osteoporosis, Rheumatoid arthritis, Sjögren syndrome)	13	52
24	Factors influencing health status or contact with health services	(Smoking)	117	468
Totals			224[a]	1665

Distribution of the patients deceased and lost to follow-up according to follow-up time			
Follow-up time	**Patients deceased**	**Patients unreachable**	**Total lost to follow-up**
First year	–	11 patients	11 patients
1-2 years	2 patients	9 patients	11 patients
2-3 years	4 patients	8 patients	12 patients
3-4 years	2 patients	7 patients	9 patients
4-5 years	3 patients	5 patients	8 patients
5-6 years	1 patient	11 patients	12 patients
6-7 years	2 patients	18 patients	20 patients
7-8 years	7 patients	19 patients	26 patients
8-9 years	3 patients	17 patients	20 patients
9-10 years	2 patients	13 patients	15 patients
10-11 years	–	12 patients	12 patients
11-12 years	1 patient	7 patients	8 patients
12-13 years	–	1 patient	1 patient
13-14 years	–	1 patient	1 patient

[a]A total of 133 patients had more than one condition.

3.5 | Binary logistic regression analysis for MBL >3 mm

There were 27 patients with implants exceeding a MBL of 3 mm. In the multivariable logistic regression model, the previous failure of a contiguous implant within the rehabilitation (OR = 3.89), biological complications (OR = 8.11) and smoking (OR = 2.72) remained significantly associated with MBL >3 mm (Table 6). No risk indicators were associated with MBL >3 mm at 15 years of follow-up (Table 6).

3.6 | Incidence and risk indicators of biological complications

Biological complications occurred at 223 of the implants (11.8%) in 120 patients (25.5%) consisting of abscess/suppuration (n = 16 implants in 12 patients) and peri-implant disease (n = 207 implants in 108 patients). In the multivariable logistic regression model, previous failure of a contiguous implant within the rehabilitation (OR = 5.56), the presence of a systemic condition (OR = 1.65) and smoking (OR = 1.75) remained significantly associated with the incidence of biological complications after adjusting for age (Table 7).

3.7 | Incidence and risk indicators of mechanical complications

Mechanical complications occurred in 139 patients in the provisional prostheses (29.5%) and 173 patients in the definitive prostheses (36.7%), with 28 patients accumulating mechanical complications in both the provisional and definitive prostheses (Table 8). In the multivariable logistic regression model, male gender (OR = 1.78; $P = 0.005$) and the type of prosthetic material used in the restoration (metal-acrylic resin: OR = 0.30, $P < 0.001$; metal-ceramic material: OR = 0.22, $P < 0.001$) remained significantly associated with the incidence of mechanical complications (Table 9).

TABLE 3 Implant cumulative survival distribution for implants supporting full-arch mandibular rehabilitations through the All-on-4 concept

Time period	Total number of implants	Number of implants lost	Lost to follow-up	Follow-up not completed	Cumulative survival rate
0-1 year	1884	7	44	0	99.6%
1-2 years	1833	5	44	0	99.3%
2-3 years	1784	5	48	0	99.1%
3-4 years	1731	4	35	0	98.8%
4-5 years	1692	1	31	0	98.8%
5-6 years	1660	4	48	0	98.5%
6-7 years	1608	3	80	0	98.3%
7-8 years	1525	3	104	0	98.1%
8-9 years	1418	2	79	0	98.0%
9-10 years	1337	15	56	0	96.9%
10-11 years	1266	9	46	269	96.1%
11-12 years	942	2	32	219	95.9%
12-13 years	689	6	4	247	94.8%
13-14 years	432	3	2	277	93.9%
14-15 years	150	1	0	81	93.0%
15-16 years	68	0	0	42	93.0%
16-17 years	26	0	0	12	93.0%
17-18 years	14	0	0	4	93.0%

4 | DISCUSSION

This study evaluated the long term outcomes of the All-on-4 concept for full-arch rehabilitation of the mandible, registering a 99.6% prosthetic survival rate and a 91.9% cumulative implant success rate up to 18 years of follow-up. To the best of the authors' knowledge these results represent the longest follow-up recorded for implant-supported immediate function restorations. The results of this study follow a pattern considering the previous publication from Maló et al[14] that evaluated the outcome of the All-on-4 concept in the mandible (with 245 patients from the sample included in the present study) with up to 10 years of follow-up and registered a 94.8% cumulative implant survival rate. Furthermore, our study included a sample of 471 patients with a follow-up beginning at 10 years and registered a cumulative implant survival rate of 96.9% at 10 years of follow-up and 93% in a follow-up up to 18 years. It is important to notice that the results of the present study comprise a sample of patients included irrespective of age, habits, or systemic compromised

TABLE 4 Implant cumulative success distribution for implants supporting full-arch mandibular rehabilitations through the All-on-4 concept

Time period	Total number of implants	Number of unsuccessful implants[a]	Lost to follow-up	Follow-up not completed	Cumulative success rate
0-1 year	1884	8	44	0	99.6%
1-2 years	1832	6	44	0	99.2%
2-3 years	1782	5	48	0	99.0%
3-4 years	1729	5	35	0	98.7%
4-5 years	1689	3	31	0	98.5%
5-6 years	1655	4	47	0	98.3%
6-7 years	1604	7	80	0	97.8%
7-8 years	1517	9	104	0	97.2%
8-9 years	1404	2	79	0	97.1%
9-10 years	1323	16	56	0	95.9%
10-11 years	1251	11	46	264	94.9%
11-12 years	930	3	32	214	94.6%
12-13 years	681	6	4	245	93.5%
13-14 years	426	3	2	274	92.6%
14-15 years	147	1	0	79	91.7%
15-16 years	67	0	0	42	91.7%
16-17 years	25	0	0	12	91.7%
17-18 years	13	0	0	4	91.7%

[a]The sum of implant failures and implant survivals (with marginal bone loss that could jeoperdize the successful outcome as defined by the success criteria).

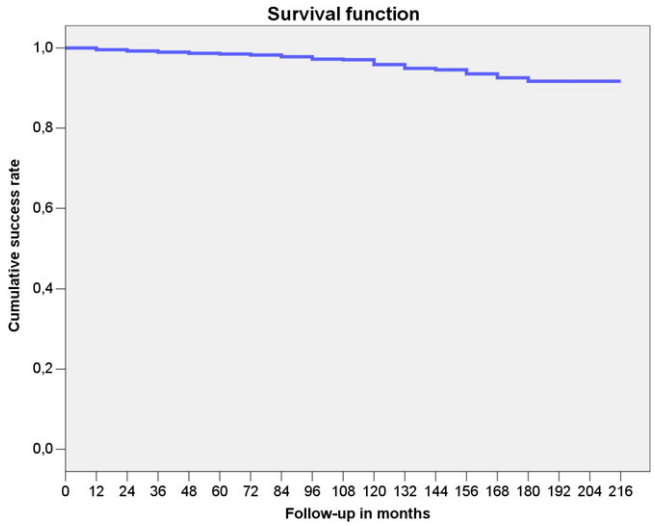

FIGURE 4 Cumulative success rate for the implants supporting All-on-4 mandibular rehabilitations: A 95.9% cumulative success rate was registered at 10 years of follow-up while a 91.7% cumulative success rate was registered up to 18 years of follow-up

conditions. Considering only the compromised status (systemic or smoking) vs the healthy status on the implants' cumulative success rate evaluation, the results yielded a 4.2% difference at 10 years and 2.8% up to 18 years in favor of the healthy status. The implant failure distribution was characterized by an increased density in the first year of follow-up (n = 12 implants lost) and a late density at 9 to 10 years of follow-up (n = 24 implants lost). Nevertheless, the late failure density can be explained by the number of implants that were classified as unsuccessful prior to the removal date (exhibiting signs of peri-implant disease with MBL surpassing the implants' middle third) but were kept in palliative treatment due to the patients' refusal to submit to surgery for reimplantation. The deleterious influence of biological complications (namely peri-implant disease) was illustrated by the regression analysis, where a fourfold increase in the hazard ratio of implant failure was registered. This result is supported by previous studies that investigated factors associated with late implant failure where peri-implant disease was considered as a major risk indicator.[22,23] In addition, other factors can partially help explain the late failure density such as the patient population with a relatively young at the time of implant placement (average of 57 years of age), and the broad inclusion criteria with the presence of smokers in the sample, a situation that was reflected on the proportional hazards analysis for implant failure. Nevertheless, nearly 70% of the late density failures (16/24 implants) occurred in peri-implant disease situations that were unresolved given the patients refusal for further surgical intervention.

The 1.7 mm of average MBL registered in the present study after 10 years of follow-up is within the reported values of other long term publications on immediate function: Ostman et al[24] reported 1.6 mm of MBL; Glauser[25] reported 1.65 mm of MBL; Degidi et al[26] reported a range between 1.93 mm and 1.98 mm (for healed sites and post-extractive sites, respectively) and Maló et al[27] reported 2.0 mm marginal bone level (specifically for the mandible). However, it is challenging to draw direct comparisons given that the studies reported the aggregated data of immediate function and 2-stage surgery;[24] of single teeth, partial and full-arch rehabilitations[24–27] and maxilla and mandible,[24–26] being this fact the illustration of the scarce existence of long term studies.

The average MBL at 15 years measured in 21 patients was 2.32 mm. Twenty-one patients represented a small sample size that given the low statistical power potentially prevented a more robust statistical evaluation, yielding no significant risk indicators retrieved from the multivariable model at 15 years. Nevertheless, these 21 patients represent the large majority of the development group from the 2003 publication[6] with an average MBL of 1.2 mm at 1 year of follow-up, rendering a 1.12 mm of MBL occurred between the first and the 15th year of follow-up at a level of 0.08 mm/year. However, 27 patients registered MBL >3 mm on their implants, an occurrence that was associated with the presence of biological complications (with an eightfold increase in the odds), smoking habits (with almost threefold increased odds compared to nonsmokers) and previous implant failure (with almost fourfold increased odds compared to patients without implant failures). Biological complications impact significantly on the success of implant-supported restorations either through MBL or by forcing implant removal and consequent failure. Moreover, the prevalence tends to increase with follow-up time. A recent systematic review investigating the prevalence of peri-implant disease disclosed a significant relation between follow-up time and the prevalence of peri-implant disease,[22] a result that previously projected almost two decades ago.[23]

The deleterious effect of smoking habits on MBL was previously reported in a study investigating the long-term outcome of implant supported restorations[24] that registered all implants with MBL at 10 years >3 mm were placed in smokers. In addition, subsequent

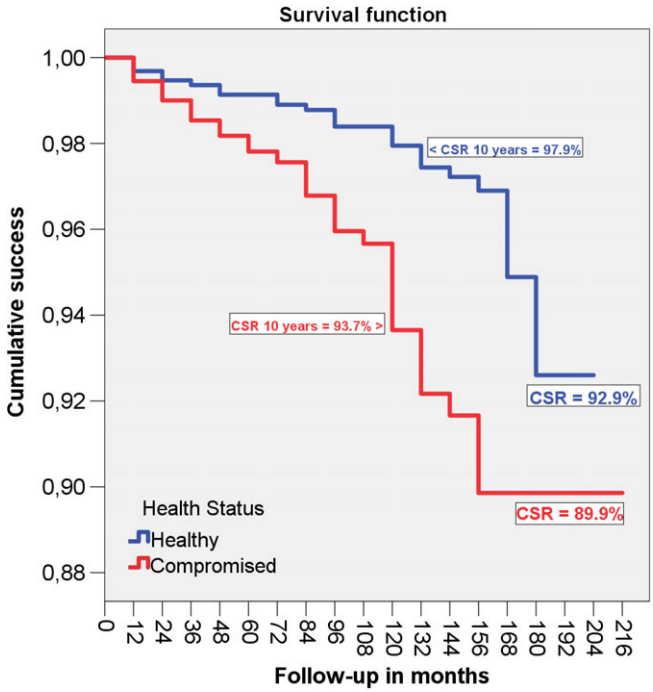

FIGURE 5 Cumulative success rate for the implants supporting All-on-4 mandibular rehabilitations. Illustrative comparison for the distribution of implant success between healthy and systemic compromised patients at 10 years of follow-up and up to 18 years of follow-up

TABLE 5 Multivariable analysis of potential hazard risk indicators associated with implant failure using the Cox proportional hazards regression model

Variables	Hazard ratio univariate	*P*	Multivariable ß	Multivariable SE	*P*	Multivariable Hazard ratio (95% CI)
Age	0.98	0.133	–0.016	0.016	0.292	0.98 (0.95, 1.01)
Gender (male)	0.39	0.028	–0.708	0.395	0.073	0.49 (0.23, 1.07)
Systemic condition	1.25	0.549				
Opposing dentition	0.97	0.749				
Cantilever size		0.056				
Absence of cantilever	1.0					
One unit cantilever	2.01	0.350	0.647	0.747	0.386	1.91 (0.44, 8.25)
Two units cantilever	3.93	0.068	1.366	0.755	0.071	3.92 (0.89, 17.22)
Prosthetic material	0.90	0.687				
Smoking	1.74	0.115	0.594	0.351	0.091	1.81 (0.91, 3.60)
Mechanical complication	1.24	0.612				
Biological complication	4.30	<0.001	1.530	0.349	<0.001	4.62 (2.33, 9.16)

investigations confirmed the higher probability for implant failure in smokers compared to nonsmoking patients[28–30] in both early and late failure considering the potential of impaired healing[31] and chronical inflammation state potentiating biological complications.[32]

Implant failures registered in the present study impacted negatively in two dimensions: The primary dimension (the failure of the implant per se) contributing to an increased probability of prosthetic failure, and the secondary dimension representing the deleterious effect on the remaining implants bearing the prosthetic load demonstrated by the significant association with both MBL >3 mm (OR = 3.89) and biological complications (OR = 5.56). However, it is important to quantify that the effect size of these associations did not correlate with the absolute implant or prosthetic failure rates that remained low in the long term outcome.

The presence of a systemic condition was significantly associated with the incidence of biological complications with a 65% increase in the odds. The level of evidence for evaluating the effect of systemic conditions on peri-implant disease is still low to draw robust conclusions.[33] A large epidemiological surveillance study evaluating the prevalence of major chronical oral conditions in a sample over 22 000 patients disclosed no association between the presence of systemic condition and peri-implant disease.[34] Nevertheless, a systematic review performing a comprehensive overview of systematic reviews and meta-analysis on peri-implant disease disclosed a higher risk for patients with uncontrolled diabetes and cardiovascular disease.[35] Considering our study, from the thirty-nine patients with systemic conditions presenting incidence of biological complications, the large majority (~80%) presented cardiovascular disease (n = 24 patients), diabetes (n = 11 patients), or both conditions (n = 4 patients). However, the interpretation of this result needs to be performed with caution given the limitation in the evaluation of the degree of control of the systemic condition that was not assessed.

Male gender was associated with an increase of 78% in the odds for mechanical complications. In the present study it was the only variable significantly associated with mechanical complications. Previous investigations disclosed greater biting forces in male patients compared to female patients[36] attributed to an average larger body mass index and significant larger facial structures.[37] The association of gender and mechanical complications in implant dentistry is not consensual. A recent risk factor model of mechanical complications in implant-supported fixed complete dentures did not register a significant association between gender and mechanical complications;[38] whereas a recent retrospective study investigating the frequency and type of complications associated with interim, immediate loaded full-arch prostheses per All-on-4 protocol did not disclose any significant association between gender and mechanical complications in interim prostheses in function for an average period of 6 months.[39] Possible explanations for these differences may rely on the study follow-up, with the present study comprising an evaluation with at least 10 years compared to the average of 6 months[39] and 3 years[38] of the previous cited investigations; or in the lack of control for other variables of interest (such as bruxism) in the present study. The type of prosthetic material used in the restoration also impacted significantly the risk of mechanical complications, with metal-acrylic and metal-ceramic prostheses exerting a protective effect when compared with acrylic-resin

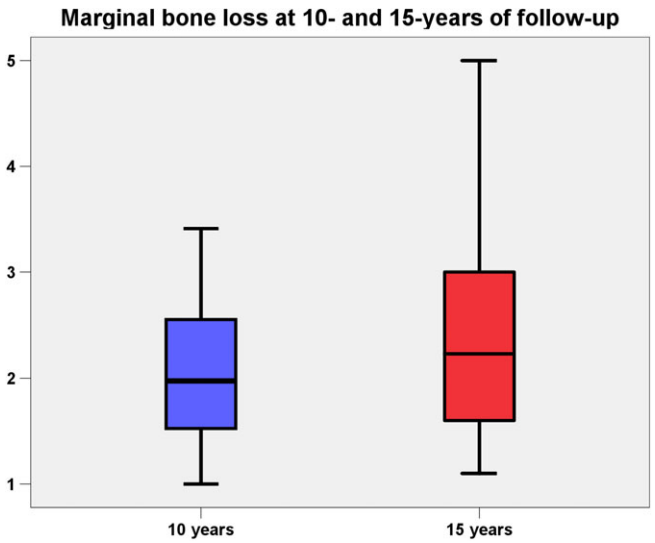

FIGURE 6 Boxplot illustrating the marginal bone loss measured in millimeters at 10- and 15-years of follow-up. At 10- and 15-years the median (horizontal black line inside the box) was 1.98 mm and 2.23 mm, respectively

TABLE 6 Binary logistic regression to evaluate the potential risk indicators for marginal bone loss >3.0 mm at 10- and 15-years

Marginal bone loss >3.0 mm at 10 years				
Factor	**OR (95% CI)**	***P***	**OR[a] (95% CI)**	***P***
Gender (female)	1.11 (0.50, 2.50)	0.796		
Age	0.98 (0.95, 1.02)	0.399		
Opposing dentition	0.92 (0.72, 1.16)	0.467		
Prosthetic material	1.53 (0.79, 2.97)	0.206		
Cantilever size	0.94 (0.50, 1.78)	0.858		
Previous implant failure	8.57 (3.27, 22.50)	<0.001	3.89 (1.34, 11.30)	0.013
Mechanical complications	0.63 (0.25, 1.58)	0.327		
Biological complications	11.57 (4.22, 31.73)	<0.001	8.11 (2.83, 23.23)	<0.001
Systemic condition	0.98 (0.40, 2.41)	0.960		
Smoking	3.41 (1.52, 7.64)	0.003	2.72 (1.12, 6.63)	0.027
Marginal bone loss >3.0 mm at 15 years				
Factor	**OR[b] (95% CI)**	***P***		
Gender (male)	1.45 (0.04, 5.21)	0.523		
Age	1.01 (0.91, 1.12)	0.850		
Opposing dentition	1.51 (0.77, 2.94)	0.233		
Prosthetic material	6.98 (0.80, 61.23)	0.080		
Cantilever size	0.81 (0.16, 4.0)	0.796		
Previous implant failure	1.0	1.000		
Mechanical complications	0.67 (0.48, 9.47)	0.765		
Biological complications	0.92 (0.07, 11.58)	0.946		
Systemic condition	0.45 (0.04, 5.21)	0.523		
Smoking	1.20 (0.15, 9.77)	0.865		

[a]OR from logistic regression analysis with pervious implant failure, biological complications and smoking included given its significance ($P < 0.20$) in the unadjusted model. $R^2 = 0.295$; Sensitivity = 18.5%; Specificity = 98.8%; Accuracy = 91.1%.
[b]Considering the small sample size and low statistical power, no factors were significant at the unadjusted model, rendering no multivariable model.

prostheses. This result would be expected from a clinical and biomechanical standpoint, as the resistance of both types of material assemblies have an increased resistance when compared to acrylic-resin alone that needs more mechanical maintenance considering the exposure to wear during a long-term follow-up. This fact is supported by a previous retrospective clinical study that evaluated tooth fractures in 161 full-arch implant-supported acrylic resin prostheses after a mean follow-up of 40 months, registering a 40% incidence rate of fractures and an increase fracture trend in men, opposing a natural arch, with cantilevers shorter than 10 mm and without mechanical retention.[40]

The limitations of the present study include the study being performed in a single center, the retrospective design and the lost-to-follow-up rate of 30% that could result in an overestimation of the implant success rate, rendering caution in the interpretation of the results. Considering the statistical analysis, further limitations include not adjusting the multivariable models to the variables

TABLE 7 Binary logistic regression to evaluate the potential risk indicators for the incidence of biological complications

Factor	OR (95% CI)	*P*	OR[a] (95% CI)	*P*
Gender (male)	1.05 (0.69, 1.61)	0.808		
Age	0.98 (0.96, 1.00)	0.053	0.99 (0.97, 1.01)	0.162
Opposing dentition	0.92 (0.82, 1.04)	0.205		
Prosthetic material	0.90 (0.64, 1.26)	0.538		
Cantilever size	0.86 (0.61, 1.20)	0.362		
Previous implant failure	6.17 (3.01, 12.62)	<0.001	5.54 (2.68, 11.47)	<0.001
Mechanical complications	0.63 (0.25, 1.58)	0.327		
Systemic condition[b]	1.44 (0.92, 2.25)	0.109	1.65 (1.02, 2.65)	0.040
Smoking	1.96 (1.25, 3.07)	0.004	1.75 (1.08, 2.83)	0.023

[a]OR from logistic regression analysis with previous implant failure, biological complications and smoking included. $R^2 = 0.111$; Sensitivity = 18.3%; Specificity = 96.3%; Accuracy = 76.4%.
[b]n = 39 patients with biological complications and systemic condition (24/39 patients with cardiovascular disease; 11/39 patients with diabetes; 4/39 patients with both cardiovascular disease and diabetes.

TABLE 8 Incidence of mechanical complications in the provisional and definitive prostheses

Complications	Number	Percentage
Provisional prostheses		
Prosthesis fracture	86	18.3%
Abutment fracture	1	0.2%
Abutment screw loosening	75	15.9%
Prosthetic screw fracture	1	0.2%
Prosthetic screw loosening	3	0.6%
Definitive prostheses		
Prosthesis fracture (acrylic resin)	107	22.7%
Ceramic crown fracture	15	3.2%
Acrylic crown fracture	75	15.9%
Cylinder fracture	5	1.1%
Artificial gingiva fracture	12	2.6%
Abutment fracture	5	1.1%
Abutment screw loosening	70	14.9%
Prosthetic screw fracture	9	1.9%
Prosthetic screw loosening	23	4.9%

Cawood and Howell classification of bone atrophy and bruxism. It is important to underline that in long term studies it is expected that the lost-to-follow-up rate to increase (~20% of the lost-to-follow-up patients deceased), but nevertheless the sample encompassed a significant number of implants with more than 15 years of follow-up.

Future research should focus on the report of more long term follow-up studies evaluating the outcome of full-arch implant-supported rehabilitations *ad modum* All-on-4 with emphasis on the definitive prostheses lifetime.

5 | CONCLUSIONS

Considering the implant and prosthetic survival and success rates, MBL and incidence of biological and mechanical complications it is concluded that the full-arch rehabilitation of the edentulous mandible *ad modum* All-on-4 is a viable treatment option validated in the long term outcome. However, biological and mechanical complications can occur. Implant failure, biological complications, MBL >3 mm, smoking and the presence of a systemic condition impacted directly and/or indirectly on the success outcome of the implant-supported rehabilitations.

CONFLICT OF INTEREST

This study was supported by Nobel Biocare Services AG, grant 2017-1534. Paulo Maló is currently a consultant for Nobel Biocare; Received previous educational fees from Nobel Biocare Services AG; Received previous scientific Grant support from Nobel Biocare Services AG; Miguel de Araújo Nobre: Received previous educational fees from Nobel Biocare Services AG; Received previous scientific Grant support from Nobel Biocare Services AG; Armando Lopes: Received previous educational fees from Nobel Biocare Services AG; Received previous scientific Grant support from Nobel Biocare Services AG; Ana Ferro: Received previous educational fees from Nobel Biocare Services AG; Received previous scientific Grant support from Nobel Biocare Services AG; João Botto: No conflict of interest.

AUTHOR CONTRIBUTIONS

Paulo Maló: conception and design of the work; interpretation of data for the work; drafting the article or revising it critically; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any parts of the work are appropriately investigated and resolved. Miguel de Araújo Nobre: the acquisition, analysis, and interpretation of data for the work; drafting the article or revising it critically; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any parts of the work are appropriately investigated and resolved. Armando Lopes: design of the work; interpretation of data for the work; drafting the article or revising it critically; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any parts of the work are appropriately investigated and resolved. Ana Ferro: design of the

TABLE 9 Binary logistic regression to evaluate the potential risk indicators for the incidence of mechanical complications

Factor	OR (95% CI)	*P*	OR[a] (95% CI)	*P*
Gender (male)	1.72 (1.17, 2.54)	0.006	1.78 (1.20, 2.69)	0.005
Age	0.99 (0.98, 1.01)	0.403		
Opposing dentition	1.12 (0.99, 1.25)	0.219		
Prosthetic material		<0.001		<0.001
Acrylic resin	1.0 (reference)			
Metal-acrylic resin	0.31 (0.20, 0.48)	<0.001	0.30 (0.20, 0.47)	<0.001
Metal-ceramic	0.22 (0.11, 0.44)	<0.001	0.22[b] (0.11, 0.44)	<0.001
Cantilever size	1.08 (0.80, 1.45)	0.618		
Previous implant failure	1.52 (0.73, 3.16)	0.268		
Biological complications	1.00	0.998		

[a]Odds ratio from logistic regression analysis with gender and prosthetic material included given its significance ($P < 0.20$) in the unadjusted model. $R^2 = 0.122$; Sensitivity = 71.3%; Specificity = 53%; Accuracy = 64.1%.
[b]An odds ratio = 0.22 for metal-ceramic material renders an odds ratio = 4.55 for acrylic resin material (odds ratio = 1/0.22 ⇔ odds ratio = 4.55).

work; interpretation of data for the work; drafting the article or revising it critically; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any parts of the work are appropriately investigated and resolved. João Botto: design of the work; interpretation of data for the work; drafting the article or revising it critically; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any parts of the work are appropriately investigated and resolved.

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How to cite this article: Maló P, de Araújo Nobre M, Lopes A, Ferro A, Botto J. The All-on-4 treatment concept for the rehabilitation of the completely edentulous mandible: A longitudinal study with 10 to 18 years of follow-up. *Clin Implant Dent Relat Res*. 2019;1–13. https://doi.org/10.1111/cid.12769