Diagnostic agreement in the assignment of the 2017 AAP/EFP World Workshop case definitions of periodontitis and peri-implant health and diseases

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XXXV Cycle
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A.A. 2021-2022

ABSTRACT

Introducing a new classification into clinical practice and research requires meticulous planning and a new way of thinking. A learning curve to understand and become acquainted with its novel nature is always needed. Therefore, it was considered of critical importance to assess whether the structure and integrated information of the 2017 AAP / EFP World Workshop Classification of Periodontal and Peri-implant Diseases and Conditions allow for a predictable definition of clinical cases. Consequently, the main objective of this thesis was to determine the level of accuracy and consistency of the clinicians in staging and grading, as well as in the definition of cases of peri-implant health and diseases.

The present cumulative dissertation consists of an introduction, three self-contained research papers and the conclusion of the thesis.

The introduction (Chapter 1) offers an overview of the topics of interest and the context in which the research was carried out. Furthermore, it outlines the rationale for the development of the present investigation.

The three research papers (Chapters 2, 3 and 4) fall naturally into two parts.

The first part (Chapters 2 and 3) included two studies focusing on the assessment of the diagnostic agreement in the definition of periodontitis cases using the staging and grading system without the aid of any implementation or with the support of a dedicated software.

In the first study (Chapter 2), thirty participants (10 periodontal experts, 10 general dentists, and 10 undergraduate students) and a gold standard examiner (selected among the authors of the 2017 AAP / EFP World Workshop case definitions of periodontitis) were asked to double-evaluate 25 fully documented cases of periodontitis. Fleiss kappa was used to estimate consistency across examiners. Intraclass correlation coefficient (ICC) was used to calculate consistency across time. Quadratic weighted kappa and percentage of complete agreement versus gold standard were computed to assess accuracy. Diagnosis was highly consistent over time. In particular, the highest ICC was provided by students for the stage (0.91), while the lowest ICC was provided by general dentists for the extent (0.79). Case

definitions were moderately reliable. Indeed, Fleiss kappa for stage, extent and grade were 0.48, 0.37 and 0.45, respectively. Accuracy was almost perfect for the stage (pair-wise comparisons with the gold standard examiner showed a mean kappa value >0.81) and moderate for grade and extent (pair-wise comparisons with the gold standard examiner showed a mean kappa value >0.41 for grade and extent). Complete agreement with the gold standard examiner for all three components of the case definition was reached in 47.2% of cases. Nevertheless, the study identified specific factors associated with lower consistency and accuracy and recognized the need for further efforts to improve the training of general dentists.

In the second study (Chapter 3), the same 10 general dentists from the previous survey were asked to independently assess 25 cases of periodontitis using a software application. Accuracy and consistency were analyzed using the same statistical methods of the earlier study. Supported by the software application, general dentists have reached substantial inter-rater agreement (Fleiss kappa was 0.818, 0.608 and 0.632 for stage, extent and grade, respectively). Assignments of stage and grade were highly accurate. More in detail, pairwise comparisons of each dentist against the reference definition resulted in at least substantial agreement in 100% of cases for stage and in 70% of cases for grade. However, complete case definitions were correctly diagnosed in only 53.6% of cases. Nevertheless, this result represented a 16% increase in accuracy over the previous attempt without any implementation tool. Additionally, the study recognized possible reasons that could lead to decreased accuracy using the software application.

The second part (Chapter 4) included one study focusing on evaluating the diagnostic agreement in assigning case definitions of peri-implant health and diseases. Indeed, the third study aimed to evaluate the consistency and accuracy in defining dental implant cases using the 2017 AAP / EFP World Workshop classification. Ten undergraduate students and 10 general dentists and a gold standard examiner (selected among the authors of the 2017 AAP / EFP World Workshop case definitions of peri-implant health and diseases) participated in this study. All examiners were provided with documentation of 25 dental implants including: years since the delivery of the prosthetic reconstruction, clinical (intra-oral photographs, probing depths, bleeding on probing and suppuration on probing) and

radiographic data. Eleven out 25 cases were also provided with baseline readings. They were asked to define all cases using the 2017 AAP / EFP World Workshop classification. Reliability among examiners was evaluated using the Fleiss kappa statistics. Accuracy was estimated using quadratic weighted kappa for pairwise comparisons between each rater and the gold standard examiner and percentage of complete agreement. Fleiss kappa for the inter-rater reliability was 0.50, which was interpreted as a moderate agreement. Agreement between each examiner and the gold standard examiner was mostly moderate (mean quadratic weighted kappa value = 0.492). Accurate case definitions were obtained in 55.0% of cases. Absence of longitudinal data impaired agreement with the reference diagnosis ($p<0.001$). Key elements to be interpreted in order to better discriminate between peri-implant health and peri-implant mucositis and between peri-implant mucositis and peri-implantitis were identified.

The conclusion of the thesis (Chapter 5) starts with an overall analysis of the main findings of the three related researches, integrating the results obtained. Moreover, it highlighted some aspects of the 2017 AAP / EFP World Workshop case definitions - recognized by the lack of agreement among examiners and the gold standard diagnosis – which should require further clarification. Finally, the future perspectives in this field are mentioned.

KEYWORDS: classification; dental implants; diagnosis; disease; health; periodontitis; periodontium; peri-implantitis; reproducibility of results

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Chapter One

Introduction

Background and rationale

Periodontitis is one of the most common diseases, together with dental caries (Wong et al., 2021). It is a multifactorial chronic inflammatory disease associated with the dysbiotic biofilm of dental plaque. Periodontitis causes progressive destruction of the connective tissue and supporting bone of the tooth and, if left untreated, leads to tooth loss and, in more advanced cases, to masticatory disfunction (Papapanou et al., 2018).

Globally, periodontitis poses a major public health challenge and affects around 40% of the adult population, with around 10% suffering from its most severe form (Eke et al., 2018; Frencken et al., 2017). Edentulism caused by periodontitis can have an influence on nutrition, quality of life, self-esteem of patients, as well as an important socio-economic impact (Tonetti et al., 2017). Furthermore, periodontitis is associated with systemic diseases, such as diabetes mellitus and cardiovascular diseases (Van Dyke et al., 2021; Wu et al., 2020), as well as with increased mortality (Romandini et al., 2020).

Similarly, peri-implant diseases are plaque-associated morbidities affecting the tissues around dental implants. While peri-implant mucositis is characterized only by inflammation of the peri-implant mucosa, peri-implantitis is also associated with the progressive loss of the bone (Berglundh et al., 2018; Schwarz et al., 2018). Furthermore, the disease progression follows a non-linear and accelerating pattern and it could determine implant loss (Derks, et al., 2016; Karlsson et al., 2019).

Depending on the case definitions, the prevalence of peri-implant mucositis is estimated to be 43% - 47% at the patient level and 29% at the implant level (Derks & Tomasi, 2015; Lee et al., 2017) while the prevalence of peri-implantitis ranges from 10% to 40% (Derks et al., 2016; Rodrigo et al., 2018; Vignoletti et al., 2019; Wada et al., 2019; Romandini et al., 2020).

It is of great importance to raise awareness of periodontal and peri-implant health and improve early diagnosis of periodontitis and peri-implant diseases to allow for appropriate treatment.

Diagnosis of periodontal and peri-implant health and diseases is assigned through classifications. The first classifications of periodontal diseases date back to the 1980s, while the latest classification of periodontal and peri-implant diseases and conditions has been introduced in 2018 by the proceedings of the World Workshop 2017 jointly held by the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) (Caton et al., 2018). This new classification includes new forms and categorization of the diseases, case definitions, and clinical criteria of each periodontal and peri-implant condition.

One of the major changes in the 2018 classification of periodontitis from the previous periodontal classification system (Armitage, 1999) is the elimination of the distinction between aggressive and chronic periodontitis. Indeed, there is no scientific evidence to support the existence of different forms of periodontitis based on clear distinctions in pathobiology (Papapanou et al., 2018), nor information of exclusive mechanisms, nor data to justify the need for specific treatment to explain this distinction (Fine et al., 2018; Lang et al., 1999; Lindhe et al., 1999; Needleman et al., 2018). Furthermore, the above-mentioned classification system caused difficulties of implementation and imprecision in the diagnosis due to the overlap in the classification of the various entities. Finally, it did not easily translate into diagnoses and treatment plans for individual patients.

The 2018 periodontitis case definition system comprises three components. First, a patient should be identified as a case of periodontitis if present: (1) interdental clinical

attachment loss (CAL) detectable at ≥2 non-adjacent teeth, or (2) buccal or oral CAL ≥3 mm with pocketing >3 mm detectable at ≥2 teeth (Tonetti et al., 2018). It was specified that the observed CAL cannot be ascribed to non-periodontal causes such as: a) gingival recession of traumatic origin; b) dental caries extending in the cervical area of the tooth; c) the presence of CAL on the distal aspect of a second molar and associated with malposition or extraction of a third molar, d) an endodontic lesion draining through the marginal periodontium; and e) the occurrence of a vertical root fracture. Secondly, on the basis of the history and specific signs and symptoms and the presence / absence of an uncommon systemic disease that compromises the host's immune response, the pathophysiological form of periodontitis should be identified among the following: a) necrotizing periodontitis (Herrera et al., 2018); b) periodontitis as a direct manifestation of systemic diseases (Albandar et al., 2018); and c) periodontitis. Third, the clinical presentation and other factors that influence clinical management, prognosis and possibly affect both oral and systemic health should be defined through the staging and grading process (Tonetti et al., 2018).

The staging system offers the possibility to go beyond the one-dimensional approach that considered only past destruction. In fact, staging is not only based on the standard dimensions of the severity and extent of periodontitis at the time of presentation but introduces the complexity dimension of the management of the individual patient. Therefore, it represents a fundamental step towards precision medicine. Table 1 provides definitions for four stages of periodontitis. Stages I and II identify cases as early as possible by recognizing the initial signs of attachment loss. On the other side of the spectrum, stage III represents more advanced cases requiring more advanced periodontal therapy and stage IV denotes complex periodontal and oral rehabilitation.

Table 1. Periodontitis stage

PERIODONTITIS STAGE		Stage I	Stage II	Stage III	Stage IV
Severity	**Interdental CAL at site of greater loss**	1-2 mm	3-4 mm	≥ 5 mm or extending to the middle third of the root	≥ 5 mm or extending to the apical third of the root
	Radiographic bone loss	Coronal third (<15%)	Coronal third (15-33%)	Extending to middle third	Extending to the apical third
	Tooth loss	No tooth loss due to periodontitis		Tooth loss due to periodontitis of ≤ 4 teeth	Tooth loss due to periodontitis of ≥ 5 teeth
Complexity	**Local**	Maximum probing depth ≤4 mm Mostly horizontal bone loss	Maximum probing depth ≤5 mm Mostly horizontal bone loss	In addition to Stage II complexity: Probing depth ≥ 6 mm Vertical bone loss ≥ 3 mm Furcation involvement Class II or III Moderate ridge defect	In addition to Stage III complexity: Need for complex rehabilitation due to: Masticatory disfunction Secondary occlusal trauma (tooth mobility degree ≥ 2 Severe ridge defect Bite collapse, drifting, flaring Less than 20 remaining teeth (10 opposing pairs)
Extent and distribution	**Add to Stage as descriptor**	For each stage, describe extent as localized (<30% of teeth involved), generalized, or molar/incisor pattern			

Since individuals may exhibit different rates of progression of periodontitis and / or risk factors, the stage should be complemented by information regarding the biological grade of the disease. Grade is based on direct or indirect evidence of disease progression and the presence of risk factors with evidence of modifying case management and prognosis (Lang et al., 2015). Table 2 illustrates periodontitis grade A (slow rate of progression), grade B (moderate rate of progresson) and grade C (rapid rate of progression).

Table 2. Periodontitis grade

PERIODONTITIS GRADE			Grade A: Slow rate of progression	Grade B: Moderate rate of progression	Grade C: Rapid rate of progression
Primary criteria	**Direct evidence of progression**	**Longitudinal data (PA radiographs or CAL loss)**	Evidence of no loss over 5 years	< 2 mm over 5 years	≥ 2 mm over 5 years
	Indirect evidence of progression	**% Bone loss/age**	< 0.25	0.25-1.00	> 1.0
		Case phenotype	Heavy biofilm deposits with low level of destruction	Destruction commensurate with biofilm deposits	Destruction exceeds expectation given biofilm deposits, specific clinical patterns suggestive of periods of rapid progression and/or early onset disease, lack of expected response to standard bacterial control therapies
Grade modifiers	**Risk factors**	**Smoking**	Non-Smoker	Smoker < 10 cigarettes/day	Smoker ≥ 10 cigarettes/day
		Diabetes	Normoglycaemic with or without prior diagnosis of diabetes	HbA1c < 7.0 in diabetes patients	HbA1c ≥ 7.0 in diabetes patients

The 2017 World Workshop on Classification of Periodontal and Peri-implant Diseases and Conditions also introduced a classification of peri-implant health and new definitions of peri-implant mucositis and peri-implantitis, based on both clinical and radiographic parameters (Tables 3, 4 and 5) (Berglundh et al., 2018).

Table 3. Peri-implant health case definition

PERI-IMPLANT HEALTH: CASE DEFINITIONS FOR DAY-TO-DAY LINICAL PRACTICE
1. Visual inspection demonstrating the absence of peri-implant signs of inflammation: pink as opposed to red, no swelling as opposed to swollen tissues, firm as opposed to soft tissue consistency;
2. Lack of profuse (line or drop) bleeding on probing;
3. Probing pocket depths could differ depending on the height of the soft tissue at the implant location. An increase in probing depth over time, however, conflicts with peri-implant health; and
4. Absence of further bone loss following initial healing, which should not be ≥2 mm.

Table 4. Peri-implant mucositis case definition

PERI-IMPLANT MUCOSITIS: CASE DEFINITIONS FOR DAY-TO-DAY LINICAL PRACTICE
1. Visual inspection demonstrating the presence of peri-implant signs of inflammation: red as opposed to pink, swollen tissues as opposed to no swelling, soft as opposed to firm tissue consistency;
2. Presence of profuse (line or drop) bleeding and/or suppuration on probing;
3. An increase in probing depths compared to baseline; and
4. Absence of bone loss beyond crestal bone level changes resulting from the initial remodeling.

Table 5. Peri-implantitis case definition

PERI-IMPLANTITIS: CASE DEFINITIONS FOR DAY-TO-DAY LINICAL PRACTICE
1. Evidence of visual inflammatory changes in the peri-implant soft tissues combined with bleeding on probing and/or suppuration;
2. Increasing probing pocket depths as compared to measurements obtained at placement of the supra-structure; and
3. Progressive bone loss in relation to the radiographic bone level assessment at 1 year following the delivery of the implant-supported prosthetics reconstruction; and
4. In the absence of initial radiographs and probing depths, radiographic evidence of bone level ≥3 mm and/or probing depths ≥6 mm in conjunction with profuse bleeding represents peri-implantitis.

For day-to-day clinical practice it may be valuable to assess the yearly rate of bone loss. This can be calculated if it is known when the implant was placed in function.

The main aspect of the current classification was to introduce a uniform definition of peri-implantitis, which had been absent until then. In fact, until 2018 there was a great variation in the clinical and radiographical parameters required to define a case affected by peri-implant mucositis or peri-implantitis. (Ramanauskaite et al., 2016)

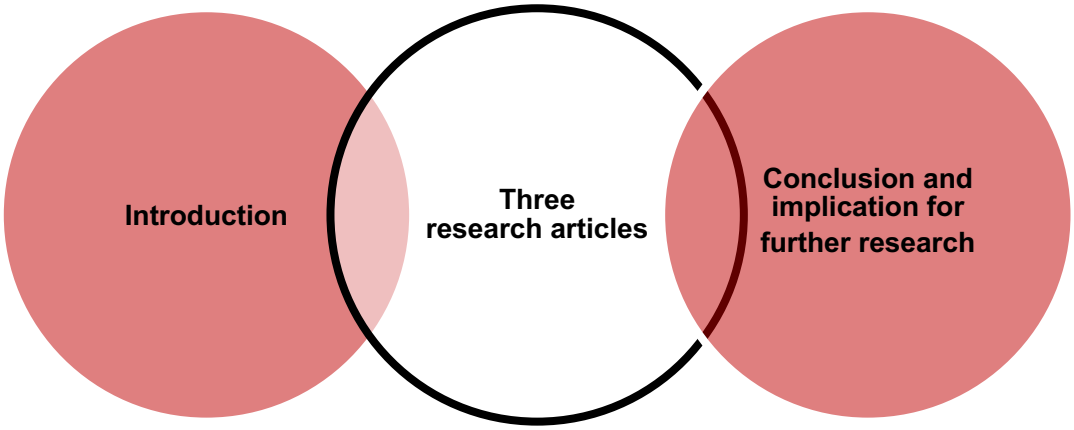
Both case definitions of mucositis and peri-implantitis would require comparison of probing depths and radiographic bone level assessed at the time of superstructure placement and 1 year after delivery of the prosthetic restoration on the implant, respectively.

Since baseline data may often not be available in clinical practice (e.g. implants placed in different settings), the 2017 World Workshop on Classification of Periodontal and Peri-implant Diseases and Conditions proposed as a secondary case definition for the diagnostic process of peri-implantitis in the absence of previous readings. Indeed, in the presence of BoP / SoP, PPD ≥6 mm and a bone level ≥3 mm apical to the most coronal portion of the intraosseous part of the implant, a diagnosis of peri-implantitis can be made (Renvert et al., 2018).

Research proposal

Introducing a new classification into clinical practice and education requires careful planning and a new way of thinking. In the absence of data available to understand whether the structure and integrated information of the classification proposed following 2017 World Workshop on Classification of Periodontal and Peri-implant Diseases and Conditions allow for a predictable classification of cases, the main objective of this research project was to determine the level of accuracy and consistency of the clinicians in staging and grading, as well as in the definition of cases of peri-implant health and disease.

Thesis outline



This cumulative PhD thesis consists of a three self-contained research papers' collection focused on a comprehensive investigation of the accuracy and consistency in defining cases according with the 2017 World Workshop on Classification of Periodontal and Peri-implant Diseases and Conditions.

The thesis falls naturally into two parts, as follows:

• **Part 1**: **Diagnostic agreement in the staging and grading of periodontitis cases.** This part (Chapters 2 and 3) consists of two scientific articles published in two renowned peer reviewed international journals, focusing on the intra-rater and inter-rater agreement when applying the 2017 World Workshop on Classification of periodontitis both with and without the aid of a designated software. Moreover, these studies assessed the inter-rater agreement of each examiner against a gold standard diagnosis to evaluate the accuracy in assigning periodontitis case definitions.

The first paper is entitled "*The staging and grading system in defining periodontitis cases: consistency and accuracy among periodontists, general dentists and undergraduate students*". It is published in *Journal of Clinical Periodontology 2021, 48, 205-215* (Impact Factor 2021: 7.478; Rank: Journal Citation Reports - Q1 (Dentistry, Oral Surgery & Medicine). This was a joint authorship (**Marini L**, Tonetti MS, Nibali L, Rojas MA, Aimetti M, Cairo F, Cavalcanti R, Crea A, Ferrarotti F, Graziani F, Landi L, Sforza NM, Tomasi C, Pilloni A) of which the candidate was the main author (first author and corresponding author). Candidate's personal contribution in this survey included: conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; visualization; writing - preparing the original draft; writing - reviewing and editing.

The second paper is entitled "*Implementation of a software application in staging and grading of periodontitis cases*". It is published in *Oral Diseases 2022, Epub ahead of print.* (Impact Factor 2021: 4.068; Rank: Journal Citation Reports - Q1 (Dentistry, Oral Surgery & Medicine). This was a joint authorship (**Marini L,** Tonetti MS, Nibali L, Sforza NM, Landi L, Cavalcanti R, Rojas MA, Pilloni A) of which the candidate was the principal author (first author and corresponding author). Candidate's personal contribution in this study comprised: conceptualization; data curation; formal analysis; investigation; methodology; project administration; visualization; writing – original draft preparation; writing – review & editing.

Part 2: **Diagnostic agreement in assigning case definitions of peri-implant health and diseases.** This part (Chapters 4) consists of one publishable scientific article to be potentially submitted in a renowned peer reviewed journal, focusing on assessing inter-rater reliability in defining dental implant cases using the 2017 AAP / EFP World Workshop classification. Additionally, the agreement of each examiner against a gold standard diagnosis was assessed to estimate the accuracy in assigning the case definition.

The third paper is entitled "*Reliability assessment of the 2017 AAP/EFP World Workshop case definitions of peri-implant health, peri-implant mucositis and peri-implantitis*". Candidate's individual contribution in this investigation included: conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; visualization; writing - preparing the original draft; writing - reviewing and editing.

The above-mentioned three papers included in the present thesis also availed themselves of the precious collaboration of some of the world's leading experts in the field of diagnosis and treatment of periodontal and peri-implant diseases, belonging to the national (University of Turin, University of Florence, University of Pisa, University of Catania) and international (University of Hong Kong, Shanghai Jiao Tong University, King's College London, Gothenburg University) academic world. Furthermore, the main authors of the new Classification of Periodontal and Peri-implant Diseases and Conditions and the

members of the 2018-19 and 2020-21 Board of the Italian Society of Periodontology and Implantology contributed to the research project.

At the end of the thesis, a final chapter (Chapter 5) discusses the results and challenges of this dissertation. Furthermore, critical appraisal of the 2017 AAP / EFP World Workshop case definitions components - identified by the lack of agreement among examiners and the gold standard diagnosis – have been discussed. Finally, the future perspectives in this field are mentioned.

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Enclosed papers

1. **Marini, L**., Tonetti, M. S., Nibali, L., Rojas, M. A., Aimetti, M., Cairo, F., Cavalcanti, R., Crea, A., Ferrarotti, F., Graziani, F., Landi, L., Sforza, N. M., Tomasi, C., & Pilloni, A. (2021). The staging and grading system in defining periodontitis cases: consistency and accuracy amongst periodontal experts, general dentists and undergraduate students. Journal of clinical periodontology, 48(2), 205–215.
https://doi.org/10.1111/jcpe.13406

2. **Marini, L**., Tonetti, M. S., Nibali, L., Sforza, N. M., Landi, L., Cavalcanti, R., Rojas, M. A., & Pilloni, A. (2022). Implementation of a software application in staging and grading of periodontitis cases. Oral diseases, 10.1111/odi.14370. Advance online publication.
https://doi.org/10.1111/odi.14370

3. **Marini, L.,** et al. Reliability assessment of the 2017 AAP/EFP World Workshop case definitions of peri-implant health, peri-implant mucositis and peri-implantitis. (to be potentially submitted in a renowned peer reviewed international Journal)

Chapter Two

The staging and grading system in defining periodontitis cases: consistency and accuracy among periodontal experts, general dentists and undergraduate students

Abstract

Aim: The objective of this study was to evaluate consistency and accuracy of the periodontitis staging and grading classification system.

Methods: Thirty participants (10 periodontal experts, 10 general dentists and 10 undergraduate students) and a gold standard examiner were asked to classify 25 fully documented periodontitis cases twice. Fleiss kappa was used to estimate consistency across examiners. Intraclass correlation coefficient (ICC) was used to calculate consistency across time. Quadratic weighted kappa and percentage of complete agreement versus gold standard were computed to assess accuracy.

Results: Fleiss kappa for stage, extent and grade were 0.48, 0.37 and 0.45 respectively. The highest ICC was provided by students for stage (0.91), whereas the lowest ICC by general dentists for extent (0.79). Pair-wise comparisons against gold standard showed mean value of kappa >0.81 for stage and >0.41 for grade and extent. Agreement with the gold standard for all three components of the case definition was achieved in 47.2% of cases. The study identified specific factors associated with lower consistency and accuracy.

Conclusions: Diagnosis was highly consistent across time and moderately between examiners. Accuracy was almost perfect for stage and moderate for grade and extent. Additional efforts are required to improve training of general dentists.

Introduction

The 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions introduced a new periodontitis case definition system (Tonetti et al., 2018). It is based on three components: (i) diagnosis of an individual as a periodontitis case; (ii) identification of the specific form of periodontitis (Albandar et al., 2018, Herrera et al., 2018); (iii) case assignment through the novel process of staging and grading (Tonetti et al., 2018).

The case definition provides a uniform description of a periodontitis patient, overcoming the difficulties of the previous classification in differentiating between aggressive and chronic periodontitis (Armitage, 1999, Lang et al. 1999). Periodontitis case definition can be easily communicated to patients or other clinicians/researchers. Furthermore, it could be relevant in assessing prognosis and may enhance individual patient management (Sanz et al., 2020).

As for all new re-classification of disease modalities, introducing a new periodontitis case definition system in clinical practice and education requires a learning curve to understand and become acquainted with its novel nature. In order to facilitate this process, empiric decision-making algorithms to guide clinicians and trainees in the assignment of cases to the proper periodontal diagnosis were suggested (Tonetti & Sanz, 2019). Furthermore, additional guidelines in the identification of potential grey zones, practical tips to help clinicians and, more recently, clarifications on how to apply the extent criterion and how to calculate tooth loss due to periodontitis were provided (Kornman & Papapanou, 2020; Sanz et al., 2020).

Since its introduction, the periodontitis case definition system progressively started to be applied in research and clinical practice. However, to the best of our knowledge, no studies have been published yet to evaluate the reliability and accuracy when defining periodontitis cases.

The objective of this study was to describe the consistency across time and across examiners in the definition of stage, extent and grade of periodontitis cases among

periodontal experts, general dentists and undergraduate dental students. The study also compared the cases definitions of examiners to a gold standard to verify their accuracy in the assignment of stage, extent and grade of periodontitis.

Materials and methods

1. Study design

The study was based on the examination of the baseline digital documentation and subsequent stage, extent and grade definition of 25 untreated periodontitis cases. All cases were evaluated by 30 examiners, equally subdivided in three groups according with their level of education and experience in periodontology. Each case was assessed twice by all the participants to calculate the consistency across time and across examiners. The assessments of each examiner were compared to those of a gold standard (MST) directly involved with the development of the staging and grading system in order to assess accuracy.

The study was conducted according to the Guidelines for Reporting Reliability and Agreement Studies (GRRAS) (Kottner et al., 2011).

2. Ethical considerations

The baseline clinical and radiographic documentation of periodontitis cases were collected in the context of routine care in the Periodontology clinic of the University of Rome from June to December 2019. Anonymized data were used in the study. All subjects had provided informed consent to the use of the collected data in the context of training and research. According with the U.S. Department of Health and Human Services (HHS) definition, this investigation is not considered human subjects research. The study protocol was approved by the Department of Oral and Maxillofacial Sciences of Sapienza, University of Rome (Prot. N. 0000598/2020). Prior to starting the study, all the examiners signed an informed consent.

3. Examiners

The following 30 participants, equally divided in three groups according to their educational level and expertise in periodontology, were selected to contribute to this study:

(i) ten final year undergraduate dental students of Sapienza, University of Rome, School of Dentistry were randomly selected using a computer-generated sequence;

(ii) ten general dentists with >10 years of clinical experience, who did not attend advanced graduate education programs in periodontology and do not exclusively focus on any specific field of dentistry in their own practice.

(iii) ten periodontal experts selected among certified periodontists by the Italian Society of Periodontology.

Furthermore, one examiner (MST) - not included in the previously described groups of participants - was selected among the authors of the case definitions for periodontitis developed in the context of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (Caton et al. 2018).

4. Procedures

4. 1. Selection and preparation of the documentation of the periodontitis cases

From 50 available fully documented periodontitis cases collected in the context of routine care, 25 were selected to ensure high quality and diagnostic precision of clinical, photographical and radiographical records by two investigators (LM and MAR) not involved in the assessments. All cases selected for this study received the diagnosis of periodontitis according to the 2017 World Workshop definition (Tonetti et al., 2018). Necrotizing forms or systemic manifestations of periodontitis were excluded from the study.

For staging the periodontitis case, full-mouth radiographs, a periodontal chart and a periodontal history of tooth loss are needed. For grading the periodontitis case previous periodontal records or, when not available, the bone/age ratio of the most affected tooth calculated on the full-mouth radiographs and information related to the presence of

recognized risk factors such as smoking and diabetes are necessary (Tonetti & Sanz, 2019). Therefore, the baseline documentation of each case provided the following information:

(a) age and gender;

(b) anamnestic data presented in a standardized format and subdivided in two sections. Section one comprised the general medical history and included any relevant systemic diseases and pharmacological treatment, as well as cigarette consumption (0, ≤10/day or >10/day). In patients with diabetes, values of glycated hemoglobin (<7% or ≥7%) acquired from the patient's medical record were provided. Section two comprised the dental history and included dichotomously recorded information (yes or no) about: 1) gingival bleeding, 2) tooth mobility, 3) dentin hypersensitivity, 4) halitosis, 5) family history of periodontitis, 6) use of interdental oral hygiene devices, 7) use of mouthwashes, 8) parafunctional habits, 9) chewing difficulties, 10) tooth migration, 11) previous orthodontic treatment, 12) previous periodontal treatment and 13) previous prosthetic treatment. Moreover, the last dental examination and professional oral hygiene procedure (≤1 year, >1 year or >3 year) and the number of tooth loss attributable to periodontitis (0, ≤4 or ≥5) were reported;

(c) nine intra-oral photographs displaying the buccal and palatal/lingual view of all sextants;

(d) full-mouth long-cone, parallel technique, periapical radiographs;

(e) a periodontal chart displaying: 1) probing depth (PD) recorded at six sites per tooth of the entire dentition; 2) clinical attachment level (CAL) recorded at six sites per tooth of the entire dentition; 3) bleeding on probing (BOP) recorded dichotomously at six sites per tooth of the entire dentition, 4) furcation involvement (FI) according to the Hamp classification (Hamp et al., 1975), 5) tooth mobility (M) according to the Miller index (Miller, 1950), 6) full-mouth plaque score (FMPS) (O'Leary et al., 1972) and 7) full mouth bleeding score (FMBS). CAL was estimated as the sum of PD and gingival margin (GM) at each site. GM measurements were performed simultaneously with the PD measurements. GM was measured by recording the distance from the cemento-enamel junction (CEJ) to the margin of the

gingiva at 6 sites on each tooth. In periodontal sites with the gingival margin located on the root and a visible CEJ, the GM was given a positive sign. In periodontal sites with no visible CEJ, the periodontal probe (PCP-UNC 15, Hu-Friedy, Chicago, IL, USA) was inserted into the periodontal pocket and angulated approximately 45° in order to manually detect the cervical line. The depth of insertion into the periodontal pocket was recorded as GM and the measurement received a negative sign.

Two slideshow presentation files containing the complete documentation of the periodontitis cases were assembled. In the two presentations there were the same twenty-five cases, but they were randomly ordered. Furthermore, a data collection file was prepared. The first presentation is provided as Supporting Information in Appendix A.

4. 2. Training of participants

Before beginning the study, all participants received a copy of the study procedures and detailed instructions. Subsequently the examiners were provided with three clinical cases, not included in the study, for explaining the case presentation and assessment modalities. When necessary, the examiners' doubts were clarified and the procedure was re-explained.

Each participant previously attended at least one course/seminar on how to apply the periodontitis case definition system. No additional training on the new classification was performed prior to the start of the study.

4. 3. Staging and grading of periodontitis cases

The three groups of participants blindly to each other and independently examined the first presentation containing the twenty-five periodontitis cases and defined stage, extent and grade of each case, according to the new classification scheme. Examiners did not have the support of any implementation tool except for the staging and grading tables for their convenience (Tonetti et al., 2018). After an interval of one week, the second presentation was examined by the three groups and all cases were again diagnosed. The examiners carried out the assessments from their own workstations and no time limits were given to the examiners to define cases. However, participants had to record the exact time necessary for staging and grading of each case.

The reference examiner examined all the periodontitis cases as well. Stage, extent and grade that he provided were chosen *a priori* and considered as the gold standard. After scoring all cases in each presentation, raters returned the data collection forms for statistical analysis.

5. Outcomes

The primary outcome was the consistency of stage, extent and grade definitions across examiners. The secondary outcomes were: (i) the consistency of stage, extent and grade definitions across time; (ii) the accuracy of the stage, extent and grade definitions**;** (iii) the scoring time.

6. Statistical analysis

The consistency of stage, extent and grade definitions across examiners, selected as primary outcome, was evaluated as an inter-examiner agreement between overall evaluators and between evaluators within each group. It was calculated based on the results of the examination of the periodontitis cases included in the first presentation using the Fleiss kappa statistics (Fleiss, 1981).

The consistency of stage, extent and grade definitions across time was estimated as intra-examiner agreement by evaluators of each group between two separate evaluations 1 week apart. It was assessed using intraclass correlation coefficient (ICC).

The accuracy of the assessments was evaluated by comparing the stage, extent and grade definitions of the cases collected in the first presentation file provided by each evaluator with those of the gold standard. Quadratic weighted kappa was calculated for each pairwise comparisons. Percentage and frequencies of complete agreement for stage, extent and grade with gold standard were also calculated. A sub-analysis was performed based on the group of the examiners, the stage, the grade and the presence of modifying factors to study the variables that could affect accuracy. In the respect of the test assumptions (Bewick et al., 2004), chi-squared test was used to determine whether there was a statistically significant difference between the expected and the observed frequencies. The significance level of statistical tests was set at 0.05.

A six-level nomenclature was used to interpret the kappa and the ICC values: poor agreement = <0.00; slight agreement = 0.00 to 0.20; fair agreement = 0.21 to 0.40; moderate agreement = 0.41 to 0.60; substantial agreement = 0.61 to 0.80 and almost perfect agreement = 0.81 to 1.00 (Landis & Koch, 1977).

In the absence of previous data in the field, the expected values of kappa are inevitably chosen arbitrarily (Sim & Wright, 2005). The more common range of kappa values in medical reliability studies is between 0.4 and 0.6 (Koran, 1975). As noted by McHugh (2012), the lowest kappa value of 0.41 may be considered adequate, even though any kappa equal or greater than 0.61 should be preferred. For this study, it was considered reasonable to expect at least kappa values of 0.41 for the consistency of stage, extent and grade definitions across examiners and of 0.61 for at least 50% of the pairwise comparisons with the gold standard.

Mean and SD of time taken for overall case definitions (stage, extent and grade) according with the different groups of examiners, the stage and the grade assigned by the gold standard and the accuracy of the diagnosis were presented. Scoring time recorded during the examination of periodontitis cases collected in the first presentation file was considered for analysis. The normality of distribution of the considered variables was evaluated with Shapiro-Wilks test or Kolmogorov-Smirnov test. In absence of normally-distributed variables, differences were compared with Kruskal-Wallis test. The significance level of statistical tests was set at 0.05

The statistical analysis was carried out by two investigators (LN and LM) using a statistical software package (IBM Corp. Released 2017. IBM SPSS Statistics for Macintosh, Version 25.0. Armonk, NY: IBM Corp.)

7. Sample size

In reliability studies, the number of subjects has a much greater impact on the precision than the number of raters does (Streiner & Norman, 2003). Therefore, it is recommended determining the number of raters based on generalizability and feasibility, then estimating the number of subjects required to achieve the desired precision (Karanicolas et al., 2009). For this investigation, the convenience number of the examiners for each of the 3 groups

was established to be 10, based on previous comparable studies (Cairo et al., 2010, Rotundo et al., 2015, Isaia et al., 2018). Then, using pairwise comparisons with a required kappa of 0.61, lower end of the 95% confidence interval (CI) for kappa as 0.28 and expected agreement 50% of the time, the required sample size was estimated to be 25 cases (Donner & Rotondi, 2010).

Results

1. Descriptive characteristics of periodontitis cases

Twenty-five periodontitis cases were examined in the present study. The sample consisted of 14 (56%) females and 11 (44%) males, aged 29 to 74 years with mean age 47.6±13.3 years. No smoking habit, cigarette consumption of <10/day and cigarette consumption of ≥10/day was observed in 17 (68%), 4 (8%) and 4 (8%) of cases respectively. The periodontitis cases were normoglycemic/no diabetes diagnosis, diabetes diagnosis with HbA1c <7% and diabetes diagnosis with HbA1c ≥7% in 22 (88%), 2 (8%) and 1 (4%) of cases respectively.

According to the diagnoses made by the gold standard examiner, the distribution of periodontitis cases by stage, extent and grade was: 2 cases were defined as stage I (8%), 4 as II (16%), 12 as III (48%) and 7 as IV (28%); 20 were assessed as generalized (80%) and 5 as localized (20%); and 10 were assigned to grade B (40%) and 15 to grade C (60%).

2. Consistency of stage, extent and grade definitions across time

The intraclass correlation coefficients (ICC) for stage, extent and grade definitions of examiners of each group are presented in table 1. Generally, consistency across time was almost perfect (ICC = 0.81 – 1.00) and higher amongst undergraduate students.

3. Consistency of stage, extent and grade definitions across examiners

Table 2 shows results of Fleiss kappa between periodontal experts, general dentists, undergraduate students and overall 30 examiners. Mostly, consistency across examiners was moderate (Fleiss Kappa = 0.41 – 0.60).

When testing in pairs, periodontal experts and students had the highest consistency for staging (Fleiss kappa = 0.60), while values for grading and extent appeared similar between groups (table 2).

4. Accuracy of stage, extent and grade definitions compared to the gold standard

Individual stage, extent and grade of the 25 periodontitis cases defined by the gold standard examiner and the 30 raters are summarized in figure 1.

Agreement with the gold standard examiner, who was assumed to provide the true definitions of stage, extent and grade is presented in table 3. The quadratic weighted kappa values were higher for stage (almost perfect agreement) than for extent and grade (moderate agreement).

Frequencies and percentage of complete agreement with the gold standard examiner are presented in table 4. Consistency with the gold standard of general dentists was significantly lower than that of the other two groups for the overall diagnosis ($p < 0.001$) and, more in detail, for stage III ($p < 0.001$), extent ($p < 0.001$) and grade B ($p < 0.001$). Among all examiners, the more severe the stage and grade the greater the possibility to get the true diagnosis ($p < 0.001$ for both stage and grade).

A high percentage of complete agreement with the gold standard was reached for the discrimination between stage I and II vs III and IV, while a progressively lower percentage of agreement was achieved for the distinction between stage II vs III, I vs II and III vs IV (figure 2).

Presence of modifying factors such as smoking and diabetes influenced agreement with the gold standard for grade. In particular, the more severe the modifier, the higher the chance of obtaining agreement with the gold standard ($p < 0.001$) (figure 2).

5. Scoring time

The mean and SD of the time taken to evaluate all cases collected in the first presentation file by the three different groups of examiners are presented in Table 5. Periodontal experts were the fastest, followed by undergraduate students and finally by

general dentists. The difference was statistically significant between the three groups ($p < 0.001$).

Table 5 shows minutes taken by all examiners for the overall diagnosis (definition of stage, extent and grade) according to the stage or the grade of the periodontitis cases (as assigned by the gold standard examiner) and according to the accuracy of the complete diagnosis. Time for case definition was significantly shorter for cases that had a higher stage ($p < 0.001$) or grade ($p = 0.003$). Finally, cases properly diagnosed by examiners were evaluated in less amount of time compared to those that were misdiagnosed ($p < 0.001$).

Discussion

The results of this study are noteworthy as they indicate that: i) general dentists performed, in general, less well than either periodontists or senior dental students; ii) clinicians performed better in the staging component of the case definition than in the newly introduced grading or extent portion; iii) less consistent and accurate diagnoses were made for borderline cases; and iv) the bone loss by age component of grading was associated with less consistency and accuracy. Taken as a whole, these findings seem to indicate that the introduction of the new classification system requires significant additional training and specific clarifications aimed at aspects characterized by lower accuracy and consistency. The good performance of dental students indicates that training is possible. Training and implementation seem to be critical as imprecision and misclassification might limit the health gains that can be obtained from a new classification (Hefti & Preshaw, 2012).

In this study, consistency of the definitions of stage, extent and grade of 25 periodontitis cases across time was almost perfect, while across examiners was moderate. This observation may question the underlying knowledge of the raters. Accuracy of stage assessments was high and greater than that of extent and grade, which were moderate. In nearly half of the cases, a complete agreement was reached with the gold standard for all three components of the case definition.

This study offers the opportunity to assess performance of users with different level of knowledge and most likely exposure to training of the new classification system. The excellent performance of dental students shows what can be achieved with incorporation of

the system into the undergraduate curriculum. Room for improvement of dental practitioners is evident and additional training seems necessary. Critical aspects for such training seem to be both extent and grade.

This analysis showed that clinicians are better at correctly discriminating more advanced stages of periodontitis (better accuracy for stage III and IV compared to stage I and II) but have difficulties in discriminating between stage III and IV. The clinical implications of this difficulty seem particularly important as it may affect communication with the patient of the complexity to manage their case.

Moderate or better agreement (0.41 based on Fleiss kappa) for stage, extent and grade, was consistently obtained only by dental students, whereas for stage and grade by periodontal experts and only for stage by general dentists. Extent obtained the lowest value of agreement among all examiners (Fleiss kappa = 0.37), probably because overall periodontitis sites distribution rather than percentage of teeth with the assigned stage was evaluated. It should be noted that the recently published clarification on how to apply the extent were not yet available to the examiners at the time of the assessments (Sanz et al., 2020). The reason why better consistency was achieved among students could be explained because they were recruited from the same institution and received uniform training.

In order to assess accuracy, each examiner's case definitions were compared with those provided by the gold standard examiner. Given the importance of providing accurate diagnoses, one expected to obtain quadratic weighted kappa ≥ 0.61 for at least 50% of the pairwise comparisons with gold standard for stage, extent and grade separately. However, it was only achieved by all examiners for stage and by periodontal experts and students for grade. With regards to the relatively low percentage of complete agreement for all three components of the case definition, it was not a surprising finding. Firstly, this may have been due to the fact that the new classification is rather "young" and, secondly, it may have been due to the large number of cases that had to be assessed in a session.

Different case definitions can have a great impact on the prevalence and the extent rates of periodontitis. In this manner, the discrepancies may influence the results and the associations presented in studies as well as over or underestimating the real need for periodontal treatment (Costa et al., 2009). Although over or the underestimation of stage as

well as of extent and grade can lead to different results, to date there is no data that suggests which of the two misalignments is worse.

In this study, none of the cases was classified as Grade A. However, this result offers an opportunity to remember how clinicians should initially assume the disease as Grade B and seek specific evidence to progress to Grade A. If in doubt, especially in the absence of direct evidence of lack of progression, clinicians should be discouraged from using Grade A at initial diagnosis.

Periodontal experts reached a diagnosis significantly faster than other groups, indicating that experience in periodontology may influence the speed in defining each periodontitis case. Although the scoring time generally seemed to be too short, the more a case showed obvious characteristics of a specific stage (in particular of stage IV) and grade (C), the less time was necessary for an exact diagnosis.

This study has several strengths. Mainly, this paper reports the first assessment of the consistency and accuracy of diagnosis that can be achieved with the new classification system. Cases were assembled in two presentation files in a randomized order after a one-week interval, to limit the effects of bias on the second examination. Documentation was shown in a uniform format that was easy to be examined. The pre-study training phase further ensured understanding of assessment methods. No time limit has been imposed for the evaluation. Data collection was simple and examiners were blinded by the case definitions of other participants. The number of examined cases was reasonably large and allowed to test the consistency and the accuracy through a wide range of manifestation of periodontitis and to perform a sub-analysis according with the case characteristics. However, further studies could require increased number of examiners.

The major limitation of this study was that all the information needed to define stage, grade and extent was assumed to be accurate and was not directly collected by each examiner. For these reasons, the effects of the individual skills in the periodontal anamnestic, clinical and radiographic examination, as well as the data selection, on the subsequent consistency in the case definition could not be estimated. However, the objective of this study was not to evaluate the diagnostic process as a whole, but rather to assess the consistency and accuracy in defining a periodontitis case when all data are available and

presumed to be correct. Another limitation was represented by the digital photographs in place of clinical inspection, even though this approach has been commonly validated in similar studies in various fields, including evaluation of aesthetic outcomes of periodontal plastic surgery (Cairo et al., 2010). Finally, the gold standard examiner was arbitrarily designated. However, he was supposed to provide the most precise case definition as one of the authors of the newly developed staging and grading system.

Conclusions

Education, practical skills and calibration might further increase both consistency and accuracy, in particular when an early periodontitis case or a borderline case in a non-smoker and/or non-diabetic patient is defined by general dentists. Further studies evaluating the ability of existing empiric decision-making tools or dedicated software to improve diagnostic skills are encouraged.

Acknowledgments

The authors are grateful to the general dentists and undergraduate dental students of the Sapienza University of Rome who participated in this study for their contribution in the role of examiners.

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Figures and figure legends

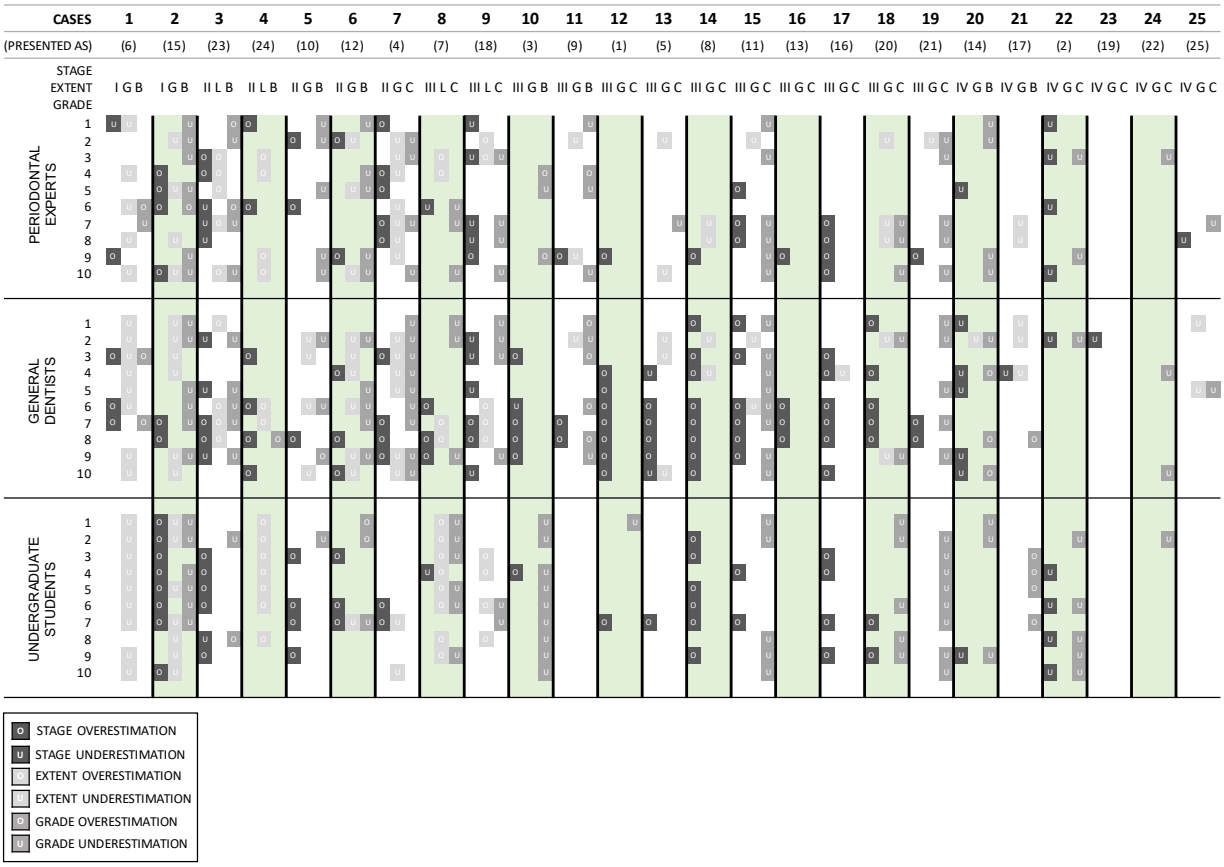

Figure 1. Individual stage, extent and grade of the twenty-five periodontitis cases defined by the gold standard examiner and comparison against periodontal experts, general dentists and undergraduate students. Cases are progressively numbered according to the increasing severity of the disease. The number assigned to each case within the first presentation file is also provided.

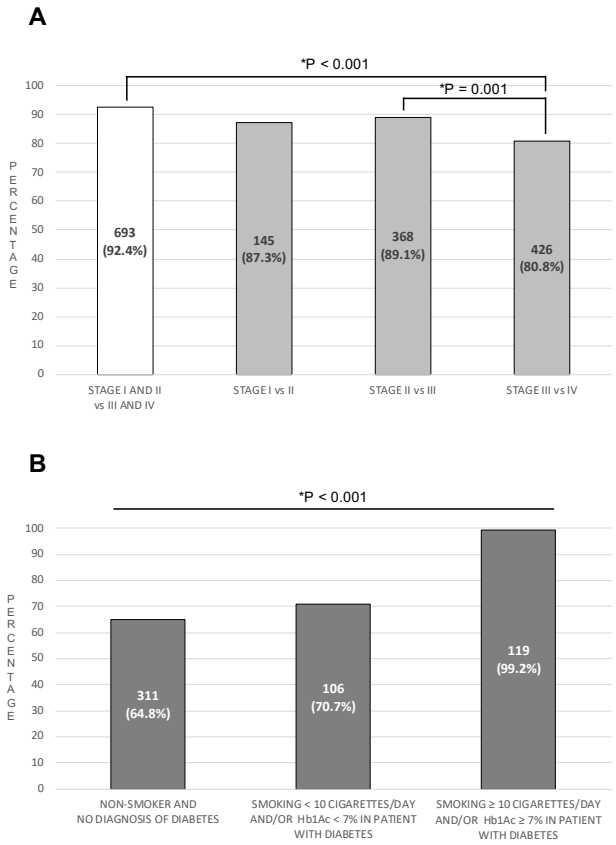

Figure 2. (A) Frequencies and percentage of complete agreement with the gold standard examiner for stage distinction between I and II vs III and IV, I vs II, II vs III and III vs IV. (B) Frequencies and percentage of complete agreement with the gold standard examiner for grade according to the presence of grade modifiers. *, statistically significant using Chi-square test; HbA1c, hemoglobin A1c values

Tables

Table 1. Intraclass correlation coefficient for different groups of examiners for stage, extent and grade

Examiners	Stage	Extent	Grade
Periodontal experts (n=10)	0.818	0.882	0.871
General dentists (n=10)	0.916	0.792	0.860
Undergraduate Students (n=10)	0.949	0.985	0.879

Table 2. Fleiss kappa statistics (95% confidence interval) for different groups of examiners, for pairs of comparisons and for overall examiners for stage, extent and grade

Examiners	Stage	Extent	Grade
Groups			
Periodontal Experts (n=10)	0.58 (0.53 – 0.61)	0.36 (0.30 – 0.42)	0.42 (0.38 – 0.46)
General dentists (n=10)	0.36 (0.32 – 0.40)	0.31 (0.25 – 0.36)	0.44 (0.39 – 0.48)
Undergraduate students (n=10)	0.65 (0.61 – 0.68)	0.64 (0.58 – 0.69)	0.52 (0.47 – 0.57)
Pairs of comparisons			
Periodontal experts - General dentist (n=20)	0.44 (0.41 – 0.45)	0.35 (0.31 – 0.37)	0.43 (0.41 – 0.45)
Periodontal experts -undergraduate students (n=20)	0.60 (0.57 – 0.61)	0.42 (0.39 – 0.45)	0.46 (0.35 – 0.48)
General dentists - undergraduate students (n=20)	0.45 (0.43 – 0.47)	0.38 (0.35 – 0.41)	0.46 (0.43 – 0.48)
Overall (n=30)	0.48 (0.47 – 0.49)	0.37 (0.35 – 0.39)	0.45 (0.43 – 0.46)

Table 3. Frequency and percentage of agreements achieved by pairwise comparisons against gold standard examiner

	Periodontal experts n (%)	General dentists n (%)	Undergraduate students n (%)	All examiners n (%)
Stage				
Slight (K = 0.01- 0.2)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
Fair (K = 0.21- 0.4)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
Moderate (K = 0.41- 0.6)	0 (0.0%)	2 (20.0%)	0 (0.0 %)	2 (6.6%)
Substantial (K = 0.61- 0.8)	1 (10.0%)	4 (40.0%)	4 (40.0%)	9 (30.0%)
Almost perfect (K = 0.81- 1.0)	9 (90.0%)	4 (40.0%)	6 (60.0%)	19 (63.3%)
Extent				
Slight (K = 0.01- 0.2)	0 (0.0 %)	2 (20.0%)	0 (0.0 %)	2 (6.6%)
Fair (K = 0.21- 0.4)	4 (40.0%)	3 (30.0%)	4 (40.0%)	11 (36.6%)
Moderate (K = 0.41- 0.6)	3 (30.0%)	4 (40.0%)	5 (50.0%)	12 (40.0%)
Substantial (K = 0.61- 0.8)	2 (20.0%)	1 (10.0%)	1 (10.0%)	4 (13.3%)
Almost perfect (K = 0.81- 1.0)	1 (10.0%)	0 (0.0 %)	0 (0.0 %)	1 (3.3%)
Grade				
Slight (K = 0.01- 0.2)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
Fair (K = 0.21- 0.4)	0 (0.0 %)	2 (20.0%)	1 (10.0%)	3 (10.0%)
Moderate (K = 0.41- 0.6)	5 (50.0%)	6 (60.0%)	4 (40.0%)	15 (50.0%)
Substantial (K = 0.61- 0.8)	5 (50.0%)	2 (20.0%)	5 (50.0%)	12 (40.0%)
Almost perfect (K = 0.81- 1.0)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)

K, quadratic weighted kappa

Table 4. Frequencies and percentage of stage, extent and grade definitions of periodontal experts, general dentists and undergraduate students consistent with those of the gold standard examiner

	Frequencies and % of complete agreement with gold standard examiner				
Variable	**Periodontal experts**	**General dentists**	**Undergraduate students**	***p* value between examiners†**	**All examiners**
Stage (I-IV)	205 (82.0%)	161 (64.4%)	204 (81.6%)	*<0.001	570 (76.0%)
Stage‡					
I	15 (75.0%)	15 (75.0%)	12 (60.0%)	0.489	42 (70.0%)
II	34 (68.0%)	33 (66.0%)	35 (70.0%)	0.912	102 (68.0%)
III	101 (84.1%)	61 (50.8%)	102 (85.0%)	*<0.001	264 (73.6%)
IV	55 (90.0%)	52 (86.0%)	55 (91.0%)	0.662	162 (89.4%)
p value between stages†	*0.017	*<0.001	*0.001		*<0.001
Extent	210 (84.0%)	191 (76.4%)	219 (87.6%)	*0.003	620 (82.6%)
Grade (A-C)	181 (72.4%)	169 (67.6%)	186 (74.4%)	0.223	536 (71.4%)
Grade‡					
A	-	-	-	-	-
B	72 (60.0%)	63 (52.5%)	87 (72.5%)	*0.006	222 (61.7%)
C	109 (83.8%)	106 (81.5%)	99 (76.2%)	0.275	314 (80.5%)
p value between grades †	*<0.001	*<0.001	0.563		*<0.001
Overall diagnosis	126 (50.4%)	94 (37.6%)	134 (53.6%)	*<0.001	354 (47.2%)

†Chi-square test
‡As assigned by the gold standard examiner
*, statistically significant

Table 5. Mean and SD of time taken for overall case definition (stage, extent and grade) according with the different groups of examiners, the stage and the grade assigned by the gold standard and the accuracy of the diagnosis

Variable	Minutes, seconds (Mean ± SD)	*P* value†
Examiners		
Periodontal experts (n=10)	1:07 ± 0:43	*<0.001
General dentists (n=10)	2:04 ± 1:04	
Undergraduate students (n=10)	1:51 ± 1:11	
Stage‡		
I (n=2)	1:52 ± 1:02	*<0.001
II (n=5)	1:54 ± 1:03	
III (n=12)	1:42 ± 1:05	
IV (n=6)	1:24 ± 1:04	
Grade‡		
A (n=0)	-	*0.003
B (n=11)	1:44 ± 0:59	
C (n=14)	1:38 ± 1:09	
Complete diagnosis‡		
Accurate	1:31 ± 1:46	*<0.001
Inaccurate	1:50 ± 1:42	

† Kruskall-Wallis test
‡ As assigned by the gold standard examiner
SD, standard deviation
*, statistically significant

Chapter Three

Implementation of a software application in staging and grading of periodontitis cases

Abstract

Objectives: The purpose of this study was to assess the diagnostic accuracy and the inter-rater agreement among general dentists when staging and grading periodontitis cases with the aid of a software application (SA) developed by the Italian Society of Periodontology and Implantology.

Materials and methods: Ten general dentists were asked to independently assess 25 periodontitis cases using the SA. Accuracy was estimated using quadratic weighted kappa and examiners' percentage of agreement with a reference diagnosis provided by a gold standard examiner. Inter-rater agreement was evaluated using Fleiss kappa statistics.

Results: The overall case definition agreed with the reference diagnosis in 53.6% of cases. The agreements for each general dentist's pairwise comparisons against the reference definition were at least substantial in 100% of cases for stage, in 70% of cases for grade and in none of the cases for extent. Fleiss kappa was 0.818, 0.608 and 0.632 for stage, extent and grade, respectively. The study recognized possible reasons that could lead to decreased accuracy using the SA.

Conclusions: Supported by the SA, general dentists have reached substantial inter-rater agreement and highly accurate assignments of stage and grade. However, complete case definitions were correctly diagnosed in slightly over half of the cases.

Introduction

A periodontitis case should be defined using the staging and grading system proposed in the 2018 Classification of Periodontal and Peri-Implant Diseases and Conditions (Caton et al., 2018; Tonetti et al., 2018). Accurate and consistent case definitions are critically important, as they can have an impact in estimating the prevalence of periodontitis (Stødle et al., 2021), in assessing the actual need for periodontal therapy (Sanz et al., 2020; Herrera et al., 2022), in the definition of the periodontal prognosis (Saleh et al., 2022; Takedachi et al., 2022) and may influence the results and associations presented in the studies (Deng et al., 2021; Goergen et al., 2021).

The consistency and accuracy among periodontal experts, general dentists and undergraduate dental students in defining periodontitis cases using the staging and grading system were first evaluated by Marini et al. (2021). It was showed that intra-rater agreement was almost perfect, whilst inter-rater agreement was moderate. In addition, the definition of stage was more accurate than those of grade or extent. In particular, the lower consistency and accuracy in the grading component was due to the assessment of the bone loss by age ratio. Overall, the ability to recognize severe forms of periodontitis (stage III and IV) was greater than that of mild forms (stage I and II). However, more difficulties were observed in discriminating between stage III and IV compared to stage I and II. General dentists showed a lower accuracy than either periodontists or senior dental students and they took longer to define each case. Ravidà et al. (2021) and Abrahamian et al. (2022) showed comparable results among periodontal experts, although a more limited number of cases and almost only severe forms of periodontitis were included in their investigations. Conversely, Gandhi et al. (2022) reported a lower rate of accurate diagnosis among undergraduate students of three different dental schools compared to the previous study. All the above-mentioned studies concluded that efforts are needed to improve diagnostic agreement in the case definition of periodontitis by identifying and clarifying the "grey zones" and implementing education and training, especially for general dentists.

Recently, a software application (SA) for digital devices was developed by the Italian Society of Periodontology and Implantology (SIdP). Using SA, clinicians have the opportunity to be guided through the staging and grading process by answering multiple choice questions with reference to the case anamnesis, clinical and radiographic data. After responding all the queries, the stage, extent and grade are automatically generated. However, this tool does not replace the diagnostic activity of the clinician and the final report must be certified by a dentist before being considered a medical diagnosis.

Up to date, the effectiveness on the diagnostic accuracy and on the inter-rater agreement as well as the time required for case definition using the SA introduced by the SIdP has not been evaluated. Therefore, the primary aim of this study is to evaluate the accuracy and the inter-rater agreement **a**mong **general dentists** in defining the stage, extent and grade of periodontitis cases with the support of a SA.

Materials and methods

1. Study design

The study was based on the case definition of 25 untreated periodontitis cases with the support of a SA introduced by the SIdP. All cases were examined by 10 general dentists to determine the diagnostic accuracy and the inter-rater agreement.

The study was conducted according to the Guidelines for Reporting Reliability and Agreement Studies (GRRAS) (Kottner et al., 2011).

2. Ethical considerations

The same documentation used for a previous study that assessed the inter-rater and intra-rater agreement and the accuracy in defining the stage, extent and grade of 25 periodontitis cases using the 2018 Classification was used for this investigation (Marini et al., 2021). Only anonymous and non-identifiable data that were not collected for the currently proposed project were used in this study, which therefore does not constitute a human subject research (U.S. Department of Health and Human Services). All subjects had provided informed consent to the use of the collected data in the context of training and research. The research protocol was approved by the Department of Oral and Maxillofacial Sciences of Sapienza, University of Rome (Prot. n. 0000203/2022). Prior to starting the study, all the general dentists signed an informed consent.

3. Examiners

The 10 general dentists who participated in the study that assessed the inter-rater and intra-rater agreement and the accuracy in defining the stage, extent and grade of 25 periodontitis cases using the 2018 Classification were recruited to participate in this study (Marini et al., 2021). The examiners were chosen from the network of private practitioners in Italy at the invitation of the study coordinator (LM). The characteristics of the participants were the following: (a) >10 years of clinical experience; (b) not having attended advanced graduate education programs in periodontology; (c) not exclusively focused on any specific field of dentistry in their own practice.

4. Procedures

4. 1. Selection and preparation of the documentation of the periodontitis cases

The same documentation of the 25 periodontitis cases used for the assessment of the reliability and the diagnostic accuracy using the staging and grading system without SA were used for this study (Marini et al., 2021). It was collected in the context of routine care in the Section of Periodontology of Sapienza University of Rome from patients suffering from periodontitis according to the definition of the 2018 Classification (Tonetti et al., 2018). Documentation was assembled in a slideshow presentation file which provided for each case:

- Personal data (age and gender);
- History of systemic diseases (glycated hemoglobin values <7% or ≥7% have been reported in patients with diabetes), pharmacological treatment and smoking (0, ≤10 / day or> 10 / day cigarette consumption);
- Dental history (including the number of teeth lost due to periodontitis (0, ≤4 or ≥5);
- Intra-oral photographs;
- Full-mouth periapical radiographs;
- Periodontal charting showing probing depth (PD), clinical attachment level (CAL) and bleeding on probing (BOP) recorded at six sites per tooth of the entire dentition, furcation involvement (F), tooth mobility (M), full-mouth plaque score (FMPS) and full-mouth bleeding score (FMBS).

A representative example of case documentation is shown in Figure 1.

For each case the reference diagnosis was considered the one assigned by a gold standard examiner without the aid of the SA (MST).

4.2. Training of examiners on the use of SA as a support to periodontitis case definition

Before beginning the study, all examiners received a copy of the study protocol. Participants had to download the SA developed by the SIdP (SIdP PowerUP, Version 1.0.2) and received a username and password for the login. Then, they received instructions for its use by one study coordinator (LM). First, participants had to select the pathway for diagnosis of "periodontitis". Then, they had to answer multiple choice questions related to the case anamnesis, clinical and radiographic data subdivided in 5 phases. The phase 1 included questions needed to define if the patient was a periodontitis case and by which form of periodontitis was affected. Phase 2 and 3 investigated, by means of specific queries, the stage of periodontitis in terms of severity and complexity, respectively. Phase 4 assessed the extent of periodontitis. Finally, phase 5 aimed at identifying, by selecting one of the

possible answers, the rate of progression of periodontitis and the presence of risk modifiers in order to establish the grade of periodontitis. Once completed, the application automatically provided a report with case definition (stage, extent and grade) of the periodontitis case. Participants were asked to train themselves through the definition of 3 periodontitis cases not included in the study with the aid of the SA.

An example of a case of periodontitis defined using SA, showing all multiple-choice questions and possible related answers, is shown in Figure 2.

4.3. Staging and grading of periodontitis cases using SA

From their own workstations, blinded to each other and without time limits, the general dentists independently assessed all the periodontitis cases using the SA and finally returned the recording file containing their diagnosis to the study coordinator (LM). They had to report also the time taken for the evaluation of each case.

5. Outcomes

5.1. Primary outcome

The primary outcome was the agreement between each general dentist and a refence diagnosis when defining stage, extent and grade of each periodontitis case using a SA as a support.

5.2. Secondary outcomes

The secondary outcomes were: (a) the inter-rater agreement between general dentists when defining the stage, extent and grade of periodontitis cases using a SA as a support; (b) the time taken for staging and grading periodontitis cases using the SA.

6. Statistical analysis

The primary outcome was estimated by evaluating the agreement between general dentists and a refence diagnosis when defining stage, extent and grade of periodontitis case using the SA. Quadratic weighted kappa was assessed for pairwise comparisons (each general dentist vs reference stage, extent and grade). The agreement of general dentists as a whole with the reference stage, extent and grade was also expressed as frequencies and percentages. Statistically significant differences between the expected and the observed frequencies were evaluated using the chi-squared test [significance level (α) = 0.05].

The inter-rater agreement was evaluated using the Fleiss kappa statistics (Fleiss, 1981). Separate analysis was performed to determine agreements for stage, extent and grade.

According to Landis & Koch (1977), the kappa values have been interpreted as follows: poor agreement = <0.00; slight agreement = 0.00 to 0.20; fair agreement = 0.21 to 0.40; moderate agreement = 0.41 to 0.60; substantial agreement = 0.61 to 0.80 and almost perfect agreement = 0.81 to 1.00. With reference to previous data in this field (Marini et al. 2021; Ravidà et al. 2021, Abrahamian et al. 2022), the expected kappa values were as a minimum of 0.61 for at least 50% of the pairwise comparisons with the reference diagnosis and at least of 0.41 for the inter-group agreement.

Average time (mean and standard deviation) taken for the diagnosis using the SA was presented. Separate analysis was also performed acccoring the stage and grade components and the accuracy of diagnosis. According with Shapiro-Wilks test or Kolmogorov-Smirnov test, in absence of normally-distributed variables, differences were compared with Kruskal-Wallis test [significance level (α) = 0.05].

A statistical software package (IBM Corp. Released 2017. IBM SPSS Statistics for Macintosh, Version 25.0. Armonk, NY: IBM Corp.) was used for the statistical analysis.

7. Sample size

The sample size was calculated on data from a previous related study (Marini et al., 2021). Consequently, the convenience number of examiners was estimated at 10 based on comparable studies (Cairo et al., 2010, Rotundo et al., 2015, Isaia et al., 2018). Regarding the number of cases of periodontitis, it was established at 25 using pairwise comparisons with a required kappa of 0.61, the lower end of the 95% confidence interval (CI) for kappa as 0.28 and the expected concordance 50% of the time. (Donner & Rotondi, 2010).

Results

1. Descriptive characteristics of periodontitis cases

The 25 cases selected for this study comprised a full spectrum of the stages of periodontitis. Descriptive characteristics of the periodontitis cases are resumed in the Table 1.

2. Agreement between general dentists and reference stage, extent and grade definitions using the SA

Figure 3 shows the reference stage, extent and grade of the 25 cases of periodontitis and, for each of them, the respective concordance, overestimation and underestimation by the 10 general dentists.

Frequency and percentage of agreements achieved by pairwise comparisons of each general dentist against reference stage, extent and grade is presented in figure 4. Mean

values of quadratic weighted kappa for stage and grade led to substantial agreement while for extent into a fair agreement.

Percentages of agreement with reference stage, extent and grade definitions are shown in table 2. Complete agreement for overall diagnosis (stage + extent + grade) was achieved in the 53.6% of cases. The less severe the stage the lower was the chance of an accurate definition ($p < 0.001$). No difference was found in the ability to get the correct diagnosis in relation to the grading ($p = 0.097$).

Frequencies and percentages of definitions by the general dentists with respect to the reference stage are presented in table 3.

Presence of grade C modifying factors (smoking ≥10 cigarettes/day and/or diabetes with HbA1c ≥7%) allowed the chance of achieving agreement with reference grade in 100% of cases. In other cases, the agreement for grade was statistically lower ($p=0.005$) (figure 5).

3. Inter-rater agreement for stage, extent and grade definitions among general dentists using the SA

Table 4 presents results of Fleiss kappa statistics. The inter-rater agreement between general dentists was almost perfect for stage, substantial for grade and moderate for extent.

4. Time taken for diagnosis using the SA

Table 5 shows the mean and SD of the time taken by the general dentists for each complete case definition (stage, extent and grade).

Data from a sub-analysis performed based on the reference stage and reference grade of periodontitis cases, as well as on the accuracy of the diagnosis, are also presented. The time to case assignment was significantly shorter when the stage and grade were higher ($p<0.001$ and $p=0.002$, respectively) and when the definitions agreed with the gold standard diagnosis ($p=0.002$).

Discussion

The main findings of this study on the use of a SA to aid general dentists in defining periodontitis cases are: i) overall diagnosis is accurate in more than half of the cases; ii) assignment of stage and grade is substantially accurate, while it is worse in terms of extent; iii) the less severe is the form of periodontitis, the harder is the chance to properly diagnose each case; iv) the inaccurate definitions are mostly due to overestimation of stage and/or grade; v) presence of high risk modifiers are positively associated to the chance of correctly assign the grade in all the cases; vi) the agreement between general dentists is high for stage and grade but it is lower for extent.

This investigation was carried out only on the general dentists since it was shown that their accuracy and inter-rater agreement was the lowest when staging and grading periodontitis cases compared to periodontal experts and dental students (Marini et al., 2021). Therefore, they could have been the ones who most benefited from support during the diagnostic process. However, more recent studies have found unsatisfactory diagnostic skills even among undergraduate students (Gandhi et al., 2022).

In this study, each examiner's case definitions were compared against a reference stage, extent, and grade, which were considered to be those assigned by an examiner gold standard. The gold standard examiner was one the authors of the staging and grading system developed in the context of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (Tonetti et al., 2018). The expected agreement (quadratic weighted kappa ≥ 0.61 for at least 50% of the pairwise comparisons) was achieved by the general dentists for stage and grade but not for extent. Otherwise, the expected value for inter-rater agreement (kappa ≥ 0.41) was obtained for all the case definition components. On the whole, the results seem to indicate that the use of the SA allows to reach satisfactory levels of accuracy and concordance. Precision in the definition of staging can translate into in the possibility of framing and planning the treatment of periodontal patients in accordance with the guidelines issued by the European Federation of Periodontology (Sanz et al., 2020; Herrera et al., 2022). Similarly, the accuracy of grading may mean being able to attribute and communicate to the patient his periodontal prognosis (Saleh et al., 2022; Takedachi et al., 2022).

The advantage offered by SA is the automated assignment of a periodontitis case definition, once the clinician has been guided step by step in considering the parameters to be evaluated in order to assign both the stage and the grade. Failure to achieve a correct diagnosis can in any case occur and be mainly due to three reasons. First reason is the incorrect answer to the multiple-choice question of the SA by the clinician due to inappropriate identification of clinical and/or radiographic data in the documentation of each case (e.g., the calculation of the bone/age ratio). The second reason relies on the fact that the application of the 2018 Classification by the SA appears to be somehow too stringent when considering the following : a) only one site necessary for any parameter to shift the stage (e.g. one site with PD> 6mm is sufficient to move from stage II to III), with a consequent tendency to overestimate the stages; b) the clinical phenotype based on destruction in relation to the amount of plaque deposits sufficient to modify the grade, making it very difficult to assign a case to grade A. In this regard, it has been suggested that upstaging due to complexity factors requires a comprehensive evaluation of these

parameters by an experienced clinician. Furthermore, the use of automated checkbox-based algorithms based on the presence / absence of isolated elements in the staging and grading process was not recommended (Kornman et al., 2020). The third reason is the extent assignment on the basis of the distribution of periodontitis and not of the stage, reducing the number of localized cases properly identified (Sanz et al., 2020). This latter aspect would require a reprogramming of the SA.

The major strength of the study is represented by the selection of the same 25 cases of periodontitis and the same 10 general dentists enrolled for the evaluations of a previously published paper on the accuracy and consistency in the definition of periodontitis cases using the 2018 Classification without any implementation tool (Marini et al., 2021). It provided an opportunity for direct comparison of results with and without the support of the SA. In this regard, the results related to staging, extent and grading showed an increase in the percentage of cases in which the definition was accurate of 10%, 6.4% and 18.4% respectively. The reached values corresponded to those obtained by periodontal experts and dental students in the previous study. The same occurs when quadratic weighted kappa values were applied. As far as the stage component, there was an improved accuracy in the definition of stage III, although there has also been a worsening in the definition of stage I. This could be partly due by the aforementioned trend to overestimation using the SA. As for the grade, it was the component that most benefited from the use of SA. In fact, there was an increase in the percentage of correct assignment in grade B. This could be affected by the almost eliminated possibility of identifying cases as grade A. Concerning the agreement between examiners, superior consistencies for stage, extent and grade were observed.

With respect to the time required for overall case definition, general dentists took a reasonable amount of time for diagnosing using the SA. It was slightly longer than the time recorded in the previous comparable study without any support (Marini et al., 2021), but seemed acceptable since the use of the SA allowed an increase in accuracy. Although a comprehensive user-friendliness evaluation of the present SA has not been carried out, which should be considered when planning further studies, the time taken for case definition could indirectly demonstrate how the use by the examiners was quite simple. Moreover, the time was shorter when diagnosing the most severe periodontitis cases (Stage IV and Grade C). This was likely due to the greater ease in detecting the data required by the application when they were more remarkable (i.e. when probing depths and clinical attachment levels were greater and radiographic bone loss more evident as well as grade C modifying factors present).

Among the limitations of this study, the small number of examiners must be considered. Even though this number has already been justified (i.e. it facilitates comparisons to a previous study), the present investigation should be understood as a pilot study. Consequently, a further survey with a larger sample size is needed to confirm and deepen the findings of the present investigation. Another weakness of the study was the additional time that general dentists had to learn the classification compared to the previous attempt. However, they were not aware about the staging and grading from the previous evaluation. Furthermore, the documentation evaluated by the examiners was collected from patients only affected by periodontitis, not offering the possibility to test the diagnostic accuracy of the SA in distinguishing between periodontal health, gingivitis and periodontitis. However, it should be mentioned that the present SA does not provide a single route for all three conditions. On the contrary, it proposes two distinct periodontal diagnostic paths to be selected a priori: "periodontal health and gingivitis" or "periodontitis". Once the "periodontitis" path is chosen, then it is asked to answer whether or not the criteria for the definition of periodontitis are met, allowing the user to continue or not the diagnostic process. If the criteria are not met, the diagnostic process is concluded and the user is asked to select the appropriate "periodontal health and gingivitis" path. In addition to the aforementioned limitations, anamnestic, clinical and radiographic data were not collected by the examiners. Therefore, the real benefit of using SA may be overestimated in this study. In fact, periodontal probing is known to require training and calibration to provide accurate measurements (Grossi et al., 1996). Similarly, reliable methods for masticatory function assessment in patients with periodontitis are not yet implemented in daily practice (Deng et al., 2022). Moreover, clinical judgment on the implications of previous tooth loss and the near-term risk of losing additional teeth could affect the staging (Sirinirund et al., 2021), just as an incomprehensive collection of medical history could impact the grading (Steigmann et al., 2021). Finally, future studies should compare the cost-benefit of using this SA with other E-Supports for periodontal diagnosis.

Conclusions

Within its limits, this study shows that the SA developed by the SIdP can be a valid tool in supporting general dentists in defining patients suffering from periodontitis. In fact, their diagnosis generally agreed. Furthermore, if staging and grading were considered separately, general dentists were extremely accurate. Conversely, when combining stage with extent and grade, their accuracy in the overall case definition was reduced.

Acknowledgments

The authors are grateful to all general dentists who participated in this study as examiners for their contributions.

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Figures and figure legends

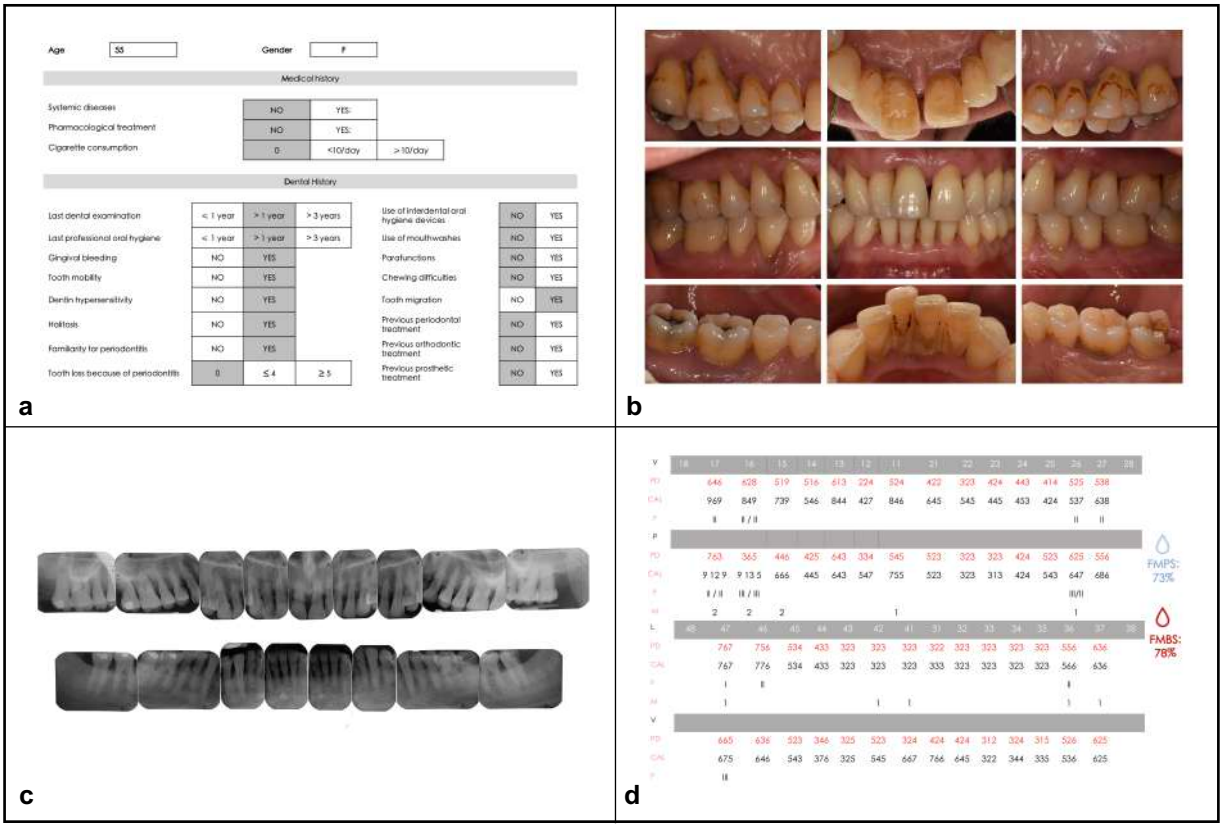

Figure 1. Representative example of documentation provided for each case. a) Personal data and general and dental history. b) Intra-oral photographs. c) Full-mouth periapical radiographs. d) periodontal charts. Abbreviations: PD = probing depth; CAL = clinical attachment level; F = furcation involvement; M = mobility; FMPS = full-mouth plaque score; FMBS = full-mouth bleeding score.

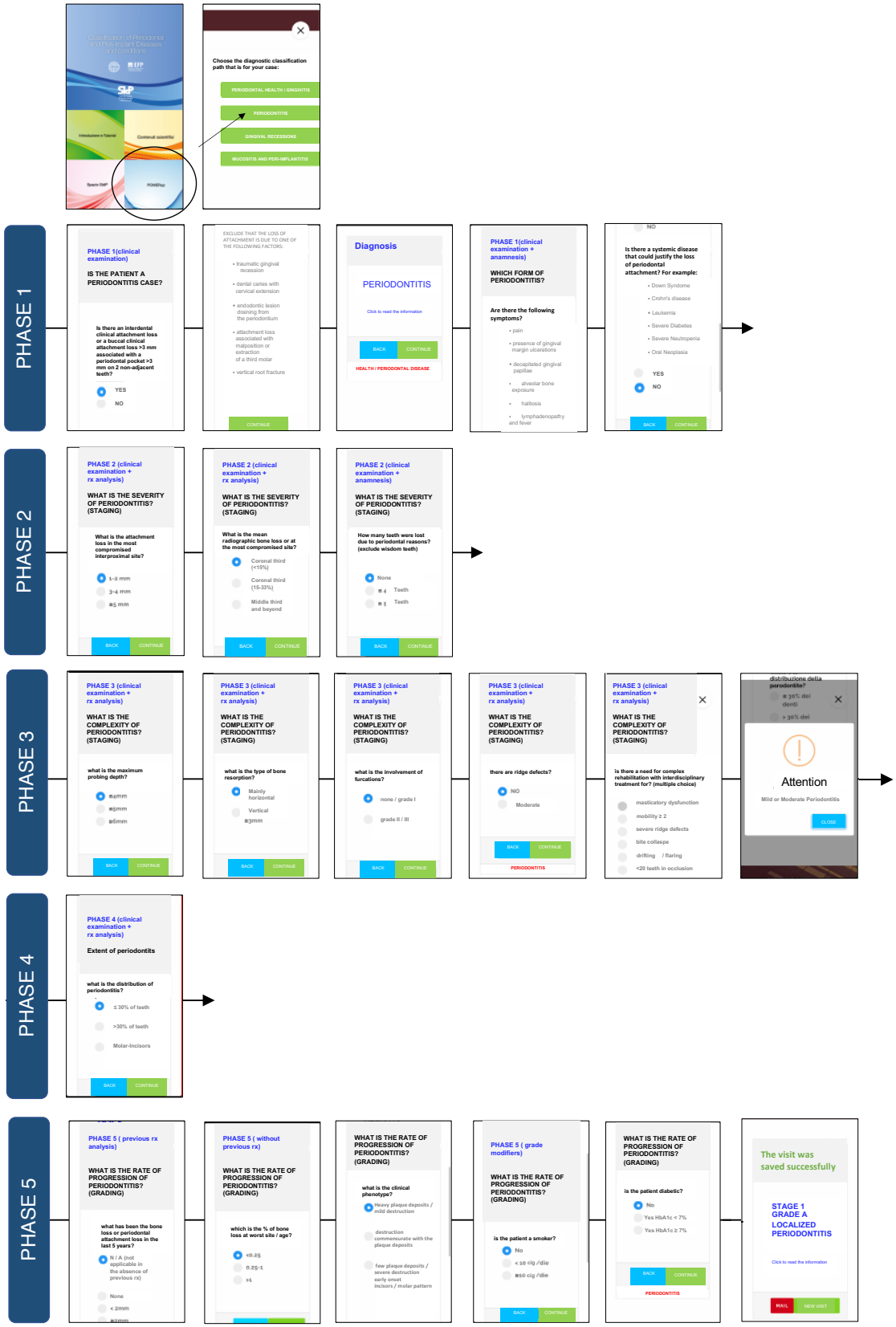

Figure 2. Example of periodontitis case defined using SA, showing all multiple-choice questions and possible related answers.

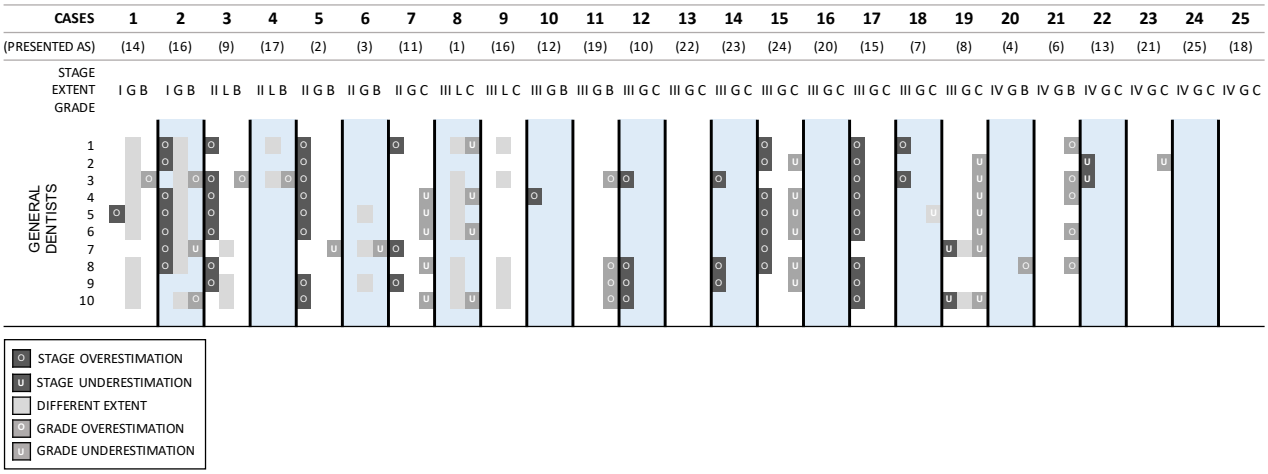

Figure 3. Reference stage, extent and grade of the twenty-five periodontitis cases and comparison against general dentists. The cases are ordered from the least severe to the most severe form of periodontitis. The order in which they were shown to the examiners is also provided.

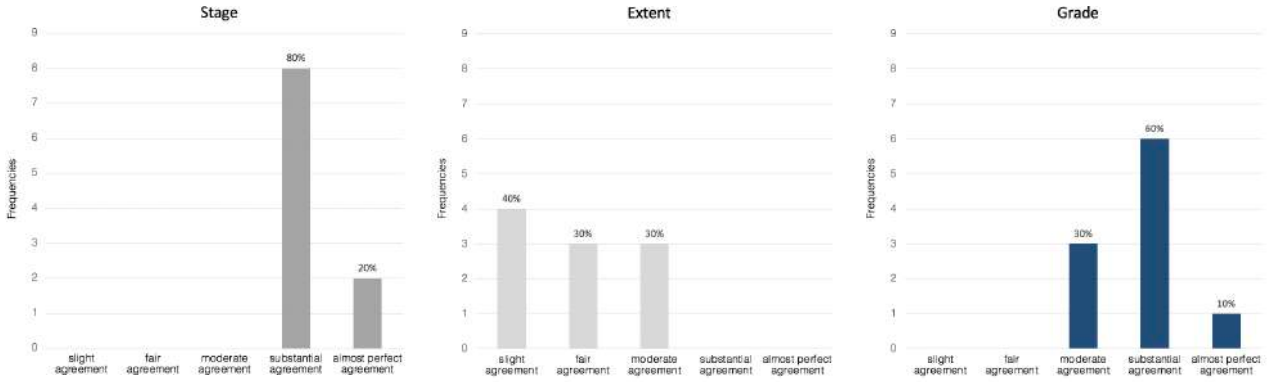

Figure 4. Frequency and percentage of agreements achieved by pairwise comparisons of each general dentist against reference stage, extent and grade using quadratic weighted kappa

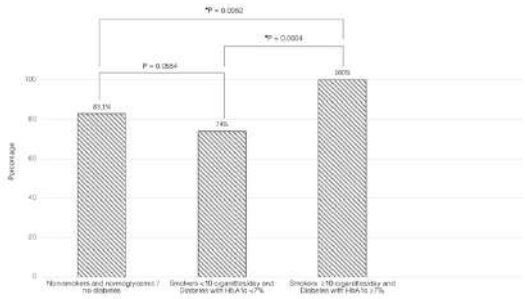

Figure 5. Percentage of complete agreement with the reference grade according to the presence of grade modifiers. *, Statistically significant using chi-square test; HbA1c, Haemoglobin A1c values

Tables

Table 1. Descriptive characteristics of the twenty-five periodontitis cases

Characteristics	Frequency (n)	Percentage (%)
Age		
(years; mean ± SD)	47.6 ± 13.3	
(years; range)	29 - 74	
Gender		
Males	11	44%
Females	14	56%
Stage		
I	2	8%
II	5	20%
III	12	48%
IV	6	24%
Extent		
Localized	4	16%
Generalized	21	84%
Grade		
A	-	-
B	10	40%
C	15	60%
Smoking		
Non-smokers	14	68%
Smokers <10 cigarettes/day	4	8%
Smokers ≥10 cigarettes/day	4	8%
Diabetes		
Normoglycemic / no diabetes	22	88%
Diabetes with HbA1c <7%	2	8%
Diabetes with HbA1c ≥7%	1	4%

Table 2. Percentages of agreement with reference stage, extent and grade definitions

Variable	% agreement with reference diagnosis
Stage (I-IV)	74.4
Stage‡	
I	60.0
II	64.0
III	70.0
IV	96.7
p value between stages†	*<.001
Extent	82.8
Localized	50.0
Generalized	89.0
p value between extent†	*<.001
Grade (A-C)	84.0
Grade‡	
A	-
B	80.0
C	87.6
p value between grades †	.097
Overall diagnosis	53.6

†Chi-square test
‡ Reference diagnosis
*, statistically significant

Table 3. Frequencies and percentages of definitions by the general dentists with respect to the reference stage

Variable	**Stage definition by the general dentists**					
Stage‡	I	II	I + II	III	IV	III + IV
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
I + II			44 (75.9%)			14 (24.1%)
III + IV			16 (8.3%)			176 (91.7%)
I	12 (60%)	8 (40%)		0	0	
II	0	32 (64%)		12 (24%)	6 (12%)	
III	2 (1.7%)	0		84 (70%)	34 (28.3%)	
IV	0	0		2 (3.3%)	58 (96.7%)	

‡ Reference diagnosis

Table 4. Fleiss kappa statistics (95% confidence interval) for stage, extent and grade

Examiners	Stage	Extent	Grade
General dentists (n=10)	0.818 (0.722 – 0.900)	0.608 (0.461 – 0.763)	0.632 (0.491 – 0.777)

Table 5. Average time taken for assessments according with different groups of examiners, stage, grade and exact diagnosis

Variable	Minutes, seconds (Mean ± SD)	*P* value†
General dentists	2:45 ± 0:57	-
Stage‡		
I	2:53 ± 0:49	<.001*
II	3:12 ± 0:54	
III	2:40 ± 0:58	
IV	2:29 ± 0:55	
Grade‡		
A	-	.002*
B	2:53 ± 0:54	
C	2:37 ± 0:59	
Complete diagnosis‡		
Accurate	2:35 ± 0:54	.002*
Inaccurate	2:56 ± 1:00	

Abbreviations: SD, standard deviation.
† Kruskal–Wallis test
‡ Reference diagnosis
*, Statistically significant

Chapter Four

Reliability assessment of the 2017 AAP/EFP World Workshop case definition of peri-implant health, peri-implant mucositis and peri-implantitis

Abstract

Aim: Recently, the 2017 AAP/EFP World Workshop on Classification of Periodontal and Peri-implant Diseases and Conditions (WWP) proposed new case definitions of peri-implant health, peri-implant mucositis and peri-implantitis, aiming to introduce a uniform classification. The purpose of this study was to evaluate the consistency and accuracy in assigning the 2017 WWP case definition to dental implants.

Methods: Ten undergraduate students and 10 general dentists and a gold standard examiner participated in this study. All examiners were provided with documentation of 25 dental implants including: years since the delivery of the prosthetic reconstruction, clinical (intra-oral photographs, probing depths, bleeding on probing and suppuration on probing) and radiographic data. Eleven out 25 cases were also provided with baseline readings. They were asked to define all cases using the 2017 WWP. Reliability among examiners was evaluated using the Fleiss kappa statistics. Accuracy was estimated using quadratic weighted kappa for pairwise comparisons between each rater and the gold standard examiner and percentage of complete agreement.

Results: Fleiss kappa for the agreement between the examiners was 0.50. Pairwise comparisons between each examiner and the gold standard showed a mean quadratic weighted kappa value of 0.492. Complete agreement with the gold standard diagnosis was

achieved in only 55.0% of cases and was even lower in the absence of reference readings ($p < 0.001$).

Conclusions: Both the reliability and accuracy in assigning case definitions to dental implants according to the 2017 WWP classification were mostly moderate. Complete agreement with the gold standard diagnosis was achieved in just over half of the cases and was unfavorably affected by the absence of longitudinal data.

Introduction

Dental implants may experience biological complications represented by inflammatory conditions of the surrounding soft and hard tissues, induced by the bacterial biofilm (Schwarz et al., 2018; Heitz-Mayfield & Salvi, 2018). The 2017 AAP/EFP World Workshop on Classification of Periodontal and Peri-implant Diseases and Conditions (WWP) proposed a new definition of these pathologies, aiming to introduce a uniform classification for peri-implant health, peri-implant mucositis and peri-implantitis (Berglundh et al., 2018; Renvert et al., 2018). Until then there was a great variation in the requirements to define a case affected by peri-implant diseases. Therefore, there was a need for standardization of peri-implant clinical and radiographical parameters in order to provide accurate diagnosis and to select the proper treatment modality in cases where disease is present (Ramanauskaite et al., 2016). The lack of consensus on the diagnosis of peri-implant health and diseases resulted in a huge heterogeneity in the reported prevalence rate of these disorders and led to misdiagnosis and over- and undertreatment of the disease (Monje et al., 2021).

According to the latest case definitions, distinction between peri-implant health and peri-implant mucositis is based on the presence or absence of the following: (a) inflamed soft tissues (e.g., red tissues, swollen tissue and soft tissue consistency); (b) bleeding (BoP) and/or suppuration (SoP) on gentle probing; and (c) increased probing pocket depth (PD). Peri-implantitis – in addition to the previous features of inflammation of the mucosa - is characterized by radiographic evidence of bone loss (Berglundh et al., 2018; Renvert et al., 2018). Baseline readings (probing depths recorded at the time of superstructure placement and radiographic bone level assessed at 1 year after delivery of the prosthetic restoration on the implant) should be taken in account in defining peri-implant health or diseases. However, as such information is often not available in clinical practice, a secondary case definition is proposed in the absence of longitudinal data (Berglundh et al., 2018; Renvert et al., 2018). This secondary case definition (bleeding on probing and / or suppuration on probing at ≥ 1 site and probing depth ≥ 6 mm and bone level ≥ 3 mm) has been shown to be able to identify moderate / severe cases of peri-implantitis while it has presented low

sensitivity in cases of early peri-implantitis (Romandini et al., 2021). Incipient cases could then be left undiagnosed and untreated by the time they would have needed less invasive treatment and show better long-term outcomes (Figuero et al., 2014; Ravidà, Saleh, et al., 2020; Ravidà, Siqueira, et al., 2020). The low sensitivity was justified by the high threshold in terms of radiographic evidence of the bone level (≥ 3 mm) as well as by the addition of PD as a parameter.

The 2017 WWP case definitions of peri-implant health and diseases encouraged comprehensive examination including both visual examinations of the peri-implant tissues and probing. Furthermore, it is recommend taking an intraoral radiograph to validate the diagnosis. However, accuracy of PD and clinical indicators of inflammation such as BoP or SoP has been the subject of intense debate (Salvi et al., 2004). Regarding PD measurement in dental implants, its diagnostic accuracy is challenged by the special characteristics of the anatomy of the peri-implant tissues compared to the anatomy of the periodontal tissue, the implant design and the implant-abutment connection (i.e., standard platform compared to the switched one, one versus two-piece implants) (Caram et al., 2014; Hermann et al., 2001; Schou et al., 2002; Lang et al., 1994). In addition, the direction, angulation and force in probing are influenced by the design of the prosthesis and the emergence profile (Cha et al., 2019). Indeed, PD assessments on implants with prosthetic reconstruction in place were less accurate than when assessed without it (Serino et al., 2013). Concerning the accuracy of BoP, this parameter has been shown to have high specificity (it was present in 91% of peri-implantitis) and moderate sensitivity (it was observed in 67% of healthy implants). False positives are likely due to mechanical fragility of the peri-implant tissues and trauma during probing (Hashim et al, 2018). Likewise, SoP appears to be an even more accurate endpoint in the diagnosis of peri-implant bone loss, although its absence does not necessarily demonstrate the absence of disease (Ostman et al., 2012; Roos-Jansaker et al., 2006).

Reliability in assessing bone height on panoramic and intraoral radiographs of implant patients showed that intra-observer agreement was high while inter-observer agreement was moderate (Kullman et al. 2007). Furthermore, the consistency of PD and clinical

measures to assess inflammation at implant sites has been described in the literature (Verhoeven et al. 2000, Koldsland et al., 2010; Lachmann et al. 2007). Merli et al. (2014) evaluated the inter-examiner agreement in the diagnosis of mucositis and peri-implantitis according to the 7th European Workshop on Periodontology's definition of perimplantitis (Lang & Berglundh 2011), which resulted merely good.

As with any classification system, it is critical to estimate consistency when applied in research and clinical practice. However, to date, the consistency of the 2017 WWP case definition of periodontitis has been assessed (Marini et al., 2021; Ravidà et al., 2021, Abrahamian et al., 2022), while no previous study assessed inter-rater reliability for the 2017 WWP case definitions of peri-implant health and diseases.

Therefore, the purpose of this survey was to evaluate the agreement between raters with different levels of education and expertise in assigning the 2017 WWP case definitions to dental implants and their accuracy against a reference diagnosis.

Materials and methods

1. Study design

This investigation was designed to test the reliability of the 2017 WWP case definition of peri-implant health, peri-implant mucositis and peri-implantitis (Berglundh et al., 2018; Renvert et al., 2018) among two groups of raters divided according to their level of education and training in implantology. Additionally, the examiners' case definitions were compared to the reference diagnosis assigned by a gold standard examiner to estimate accuracy. Photographs, clinical and radiographic data of twenty-five implant cases were used for this study. The study was prepared following the Guidelines for Reporting Reliability and Agreement Studies (GRRAS) (Kottner et al., 2011)

2. Ethical considerations

The documentation of the twenty-five implant cases was collected in the context of routine care at the Section of Periodontology of the Sapienza University of Rome from subjects who received implant-supported restorative therapy. Only anonymous and non-identifiable data were used in this study. Patients whose cases were included in this survey provided their informed consent to use the collected data for training and research purposes. The protocol was in accordance with the Declaration of Helsinki of 1975, revised in Tokyo in 2013.

3. Examiners

A total of 20 participants from different education and training in implant dentistry were selected as follows:

(a) 10 fifth year undergraduate dental students randomly among those at the Sapienza University of Rome.

(b) 10 general dentists (clinician whose practice is not limited to a specific area and who is not certified by a recognized specialty board) with at least 10 years of clinical experience in general/implant dentistry among those graduated at Sapienza University of Rome.

All examiners were informed of the purpose of the study and their participation was voluntary. Furthermore, their case definitions were collected anonymously.

4. Gold standard examiner

A different examiner was designated, among the participants in Working Group 4 on the Classification of Peri-Implant Diseases and Conditions in the context of the AAP / EFP 2017 World Workshop (Berglundh et al., 2018), to assign the "true" diagnosis to all cases. The reference case definitions he provided were compared with those of the examiners who participated in the reliability assessment to estimate their accuracy.

5. Clinical cases

The examiners were provided with a single document (Adobe Acrobat Pro DC for Mac ©, version 2021.005.20058) containing twenty-five numbered slides. Each slide showed one implant case, providing the clinical and radiographic data needed for case definition through indirect evidence according to the 2017 WWP (Renvert et al., 2018), including:

- time (years) from the delivery of the implant-supported prosthetics reconstruction;
- probing depth (mm) measured at six sites per implant with a manual periodontal probe[1];
- bleeding on probing (BoP) (no/yes) recorded at six sites per implant within 15 s following probing;
- suppuration on probing (SoP) (no/yes) assessed at six sites per implant within 15 s following pocket probing;
- two intraoral photographs (one buccal and the other palatal / lingual) showing the clinical aspect of the dental implant and the soft peri-implant tissues;
- a long cone, parallel technique, periapical radiograph of the dental implant. To allow assessments of the bone level, the radiograph was provided with a millimeter ruler whose beginning was at the level of the most coronal point of the intraosseous part of the implant. The implant length was used for the ruler calibration.

Eleven out 25 cases were also provided with baseline readings obtained from patient files. These longitudinal data allowed case definition through direct evidence according to 2017 WWP (Renvert et al., 2018) and included:

- probing depth (mm) measured at six sites per implant with a manual periodontal probe[1] at the time of superstructure placement;
- a long cone, parallel technique, periapical radiograph of the dental implant taken at 1 year after delivery of the prosthetic restoration.

A representative example of case documentation is shown in Figure 1.

[1] PCP15 (Hu-Friedy, Chicago, IL, USA)

All clinical measurements were performed by a single calibrated investigator who was not involved in the assessment of reliability. Similarly, intraoral photographs and radiographs were taken by clinicians other than examiners.

The clinical cases were collected by a member of the study team among the subjects who received restorative therapy supported by implants who were visited at the Section of Periodontology of the Sapienza University of Rome.

The document including all 25 clinical cases is provided as Supporting Information in Appendix B.

***6.* Assignment of case definitions**

Prior to the distribution of the cases for evaluation, the examiners were provided with detailed information on the study procedures. In addition, they received a pre-designed spreadsheet in which to write down their diagnosis of peri-implant health, peri-implant mucositis or peri-implantitis for each case.

None of the participants were aware of the cases prior to the evaluation, nor did they receive any other information or guidance during the assessment.

Examiners accomplished their tasks independently and blindly to each other, from their own workstations and without time limitations.

Training and calibration on AAP / EFP 2017 World Workshop case definition of peri-implant health and diseases were intentionally not provided to examiners prior to the study. However, during the assessments, all participants were allowed to access a summary of the parameters for case definition of each peri-implant health status, prepared by a study team member.

6. Outcomes

Reliability between the case definitions provided by each examiner and those assigned by the gold standard examiner was considered as primary outcome. The secondary outcomes, considered as potential explanatory outcomes, were: (a) the reliability among examiners (overall and by group) in defining peri-implant health status; (b) agreement with the gold standard case definition in relation to the presence or absence of baseline readings and the education and clinical experience of the observers.

7. Data analysis

Continuous variables were described by means (±standard deviation) and categorical variables by frequency distributions (percentage).

The primary outcome -reliability between each examiner and the gold standard examiner- was estimated by quadratic weighted kappa (Cohen, 1968). The inter-examiner reliability was evaluated using the Fleiss kappa statistics (Fleiss, 1981).

The kappa values have been interpreted as follows: poor agreement = <0.00; slight agreement = 0.00 to 0.20; fair agreement = 0.21 to 0.40; moderate agreement = 0.41 to 0.60; substantial agreement = 0.61 to 0.80; and almost perfect agreement = 0.81 to 1.00 (Landis & Koch, 1977).

Statistically significant differences between expected and observed frequencies in complete agreement with the reference diagnosis according to the examiner group and the presence or absence of baseline readings were assessed using the chi-squared test. The significance level (α) was set at 0.05.

All analyses were performed using a dedicated software[2].

[2] IBM SPSS Statistics (IBM SPSS Statistics for Macintosh, Version 25.0. Armonk, NY: IBM Corp)

8. Sample size

Number of clinical cases required for kappa statistics for two observers (each examiner versus gold standard examiner) and 3 categories (peri-implant health, peri-implant mucositis and peri-implantitis) was estimated using the confidence interval perspective, using the function "CI3Cats" of the package "kappaSize" for R environment for statistical computing[3] (Rotondi, 2013). The anticipated value of kappa was set at 0.50, the lower bound of the CI95% was set at 0.20 and upper bound at 0.80. In addition, the anticipated prevalence of peri-implant health, peri-implant mucositis and peri-implantitis was set respectively at 0.30, 0.40 and 0.30. Using the above-mentioned parameters, a minimum sample of 25 subjects was necessary.

The number of examiners was based on generalizability and feasibility, then according to comparable studies (Isaia et al., 2018; Marini et al., 2021; Barootchi et al., 2022; Marini et al. 2022) 20 evaluators (10 per group) were included in this investigation.

Results

1. Descriptive characteristics of implant cases

Table 1 provide descriptive data of the study population of implants.

2. Agreement with gold standard case definition

Table 2 provides the case definitions assigned by the gold standard examiner and the rationale for each diagnosis.

Figure 2 shows the relative proportions of peri-implant health, peri-implant mucositis and peri-implantitis assigned by examiners for every case along with the case definitions provided by the gold standard examiner.

[3] R: R Foundation for Statistical Computing, Vienna, Austria.

Values of quadratic weighted kappa for pairwise comparisons of each examiner against gold standard examiner are presented in Table 3. Mean value of quadratic weighted kappa (k = 0.492) was interpreted as moderate agreement. The frequencies and percentages of poor, slight, fair, moderate and substantial agreements achieved by pairwise comparisons are shown in Figure 3. The general dentists were more accurate than undergraduate dental students, with a higher percentage of examiners showing moderate (8 vs 6) or substantial (2 vs 1) agreement with the gold standard.

Frequencies and percentages of complete agreement with gold standard case definitions are shown in figure 4. Complete agreement with gold standard diagnosis was achieved in the 55.0% of cases. There was a non-statistically significant difference in the ability to assign an accurate case definition based on examiner education and clinical experience, despite general dentists performing better then undergraduate students (58.0% vs 52.4%, p = 0.208). Conversely, the presence or absence of baseline readings statistically significantly affected the possibility of complete agreement with the gold standard examiner (61.3% vs 50.3%, respectively; p <0.001). (figure 4)

3. Inter-examiner agreement

Table 4 presents the results of the Fleiss kappa statistics relating to the agreement between the overall group of examiners and between each group of observers (undergraduate students and general dentists).

Inter-rater reliability was simply moderate [k = 0.50 (0.47, 0.52)], with comparable results within the two groups [undergraduate students: k = 0.46 (0.41, 0.50); general dentists: k = 0.53 (0.48, 0.57)].

Furthermore, the presence or absence of baseline readings did not appear to affect agreement among all examiners [presence: k = 0.44 (0.39, 0.50); absence: k = 0.48 (0.43, 0.53)].

Discussion

Classifications should be simple, exhaustive and useful (Pini-Prato, 2011). In addition, case definitions should be accurate and reproducible, as inconsistent assessment can generate serious consequences, including misdiagnosis and inappropriate treatment (Hefti & Preshaw 2012). Therefore, this study was of great interest, as it aimed to assess for the first time the reliability and accuracy in assigning the case definition of peri-implant health, peri-implant mucositis and peri-implantitis according to 2017 WWP. The main findings of this study included the following: (1) the examiners were accurate in just over half of the cases, mostly showing moderate agreement with the reference diagnosis; (2) accuracy was more affected by presence or absence of longitudinal data than by the examiner training and clinical experience; (3) reliability among examiners was moderate, with comparable results in each group.

With respect to the primary outcome, pairwise comparisons between each examiner and the gold standard showed a mean quadratic weighted kappa value of 0.492. It was interpreted as moderate agreement and was close to the expected value. Merli et al. (2014) previously clinically assessed the inter-rater agreement in the diagnosis of peri-implant disease according to the definition of the 7th European Workshop on Periodontology (Lang & Berglundh, 2011). In their study, the agreement between three clinicians experienced in implant diagnosis and therapy in the evaluation of 27 dental implants was substantial (Fleiss k-statistic with square weight was 0.66, CI95%: 0.45–0.87). The higher reliability with respect to the present survey could be justified not only by the differences in the case definitions (7th European Workshop on Periodontology vs 2017 WWP), but also by the dissimilar number of observers and their experience in implantology.

Using the diagnostic criteria of the 2017 WWP case definitions of peri-implant health and diseases, some inconsistencies arose se in presence of specific clinical situations.

A frequent clinical scenario has been the presence of single or very limited positive sites for bleeding on probing in otherwise healthy implant cases. Technically, the presence of BoP can change the diagnosis from a healthy implant to mucositis. However, bleeding at implant sites could be often the result of trauma rather than inflammation, due to the mechanical fragility of the peri-implant tissues. Moreover, it could be influenced by various factors such as probing force, the type of probe and the technique used, quantitative and qualitative aspects of the peri-implant biofilm, modifying factors related to the patient and the site that alter the conditions of the host and the presence of prosthesis or its overhangs / convex profile that prevent an adequate assessment (Ericsonn et al., 1986; Pontoriero et al., 1994; Zitzmann et al., 2001; Atassi, 2002; Salvi et al., 2012; Farina et al.,2017; Merli et al., 2017; Monje et al., 2018). Furthermore, although the presence of BOP at the implant site is associated with a high negative predictive value and high sensitivity (Jepsen et al., 1996; Luterbacher et al., 2000), the number of positive BOP sites around an implant that was found to be the strongest predictor of advanced disease progression ranges from three to four (Karlsson et al., 2019). Nevertheless, non-dichotomous scales are recommended to classify bleeding on probing to improve accuracy in diagnosing inflammatory conditions (e.g., mucositis or peri-implantitis) (Monje et al., 2021). In the present study, cases exhibiting only 1-2 sites positive for bleeding were frequently considered healthy by the examiners, underestimating the presence of peri-implant mucositis (e.g., cases number 12 and 23).

Three millimeters of bone loss are required - along with PD ≥6 mm and bleeding on probing - to define cases of peri-implantitis according to the WWP 2017 classification. This threshold has been explained because it is generally perceived that after implant placement and initial loading, part of the crestal bone height is lost (between 0.5 and 2 mm) during the healing process. However, this definition showed low sensitivity, especially for the early / incipient forms (Romandini et al., 2021). Furthermore, in the present study, positive cases for PD ≥6 mm and bleeding, but exhibiting bone level equal to 1 or 2 mm, in the absence of longitudinal data, lead to inconsistencies in the diagnosis due to the difficulty of observers in discriminating between mucositis and peri-implantitis (e.g., case number 10). Additionally, the diagnosis of cases without longitudinal data was statistically significantly

less accurate ($p < 0.001$). This result confirms the importance of baseline readings in the diagnosis of peri-implant diseases and suggests considering a possible reduction in the threshold for bone level (e.g. from ≥3 mm to ≥2 mm) in the absence of longitudinal data.

The absence of bleeding combined with the presence of one or both of the other parameters required for secondary case definition (probing depth ≥ 6 mm and bone level ≥ 3 mm) could lead to difficulties in assigning the correct case definition using indirect evidence. These scenarios, in fact, do not allow the diagnosis of peri-implantitis or mucositis and should be considered as peri-implant health in cases previously affected by peri-implantitis or with deep mucous tunnel. Similarly, in cases displaying gingival recession, negative for probing depth ≥ 6 mm, but positive for bleeding on probing and bone level ≥ 3 mm, diagnosis of peri-implantitis in absence of longitudinal data should not be made. In the present investigation, considering the gold standard diagnosis, there were no implant cases with the characteristic described above but it is supposed that they would have impaired reliability and accuracy among examiners.

Incongruities and inaccuracies also arose when clinicians were asked to define implant cases that showed the presence of isolated clinical and / or radiographic signs in different implant sites. For example, in cases where an implant was positive for bleeding and negative for probing depth and bone loss in the mesio-buccal aspect and at the same time negative for bleeding and positive for probing depth and bone loss in the disto-palatal aspect. Indeed, these cases should theoretically be diagnosed as peri-implantitis.

The main strength of this investigation was the presence of a wide spectrum of clinical scenarios, comprising several cases for each peri-implant health status. Furthermore, borderline cases that showed specific features that posed diagnostic challenges and resulted in more variance among raters were included in this study.

Among the limitations of this research, it should be considered that the clinical and radiographic data to be evaluated to define each implant case were not collected by

observers. Indeed, the aim of the present study was to assess the consistency and accuracy in the assignment of the case definition according to the 2017 WWP classification rather than in the overall diagnostic process. The latter, in fact, is further affected by reliable measurements of probing depths, bleeding on probing, as well as the availability of good quality radiographs (Koldsland et al., 2010, Merli et al., 2014). It should also be mentioned that probing was performed by a single member of the study team not involved in the reliability assessment without removing the implant restorations, which has previously been shown to result in a reduced correlation between marginal bone levels and PD (Serino et al., 2013). A further weakness was represented by the inclusion of only undergraduate dental students and general dentists, not allowing to test the reproducibility among recognized experts in implantology. Moreover, the brand and characteristics of implants were not standardized, but it could have provided a more realistic representation of clinical practice. Regarding the number of examiners, although it may seem limited, it is very similar to those of other studies that have evaluated reproducibility in other fields (Isaia et al., 2018; Marini et al., 2021; Barootchi et al., 2022; Marini et al. 2022). Furthermore, in reliability studies, the number of clinical cases has a much greater impact on consistency than the number of examiners (Streiner & Norman, 2003).

Conclusions

In summary, both the reliability and accuracy in assigning the case definition of peri-implant health, peri-implant mucositis, and peri-implantitis according to the 2017 WWP classification were mostly moderate. Complete agreement with the gold standard diagnosis was achieved in just over half of the cases and was unfavorably affected by the absence of longitudinal data. Proper interpretation of the presence of isolated sites with bleeding / suppuration on probing and the precise assessment of the radiographic bone level were key elements in discriminating respectively between peri-implant health and peri-implant mucositis and between peri-implant mucositis and peri-implantitis.

Acknowledgment

The authors are grateful to the participants of this study for their contribution in the role of examiners.

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Figures and Figure Legends

Figure 1. Representative examples of documentation provided for each dental implant in presence (case 1) or in absence (case 2) of baseline readings. PD, probing depth; BoP, bleeding on probing; SoP, suppuration on probing

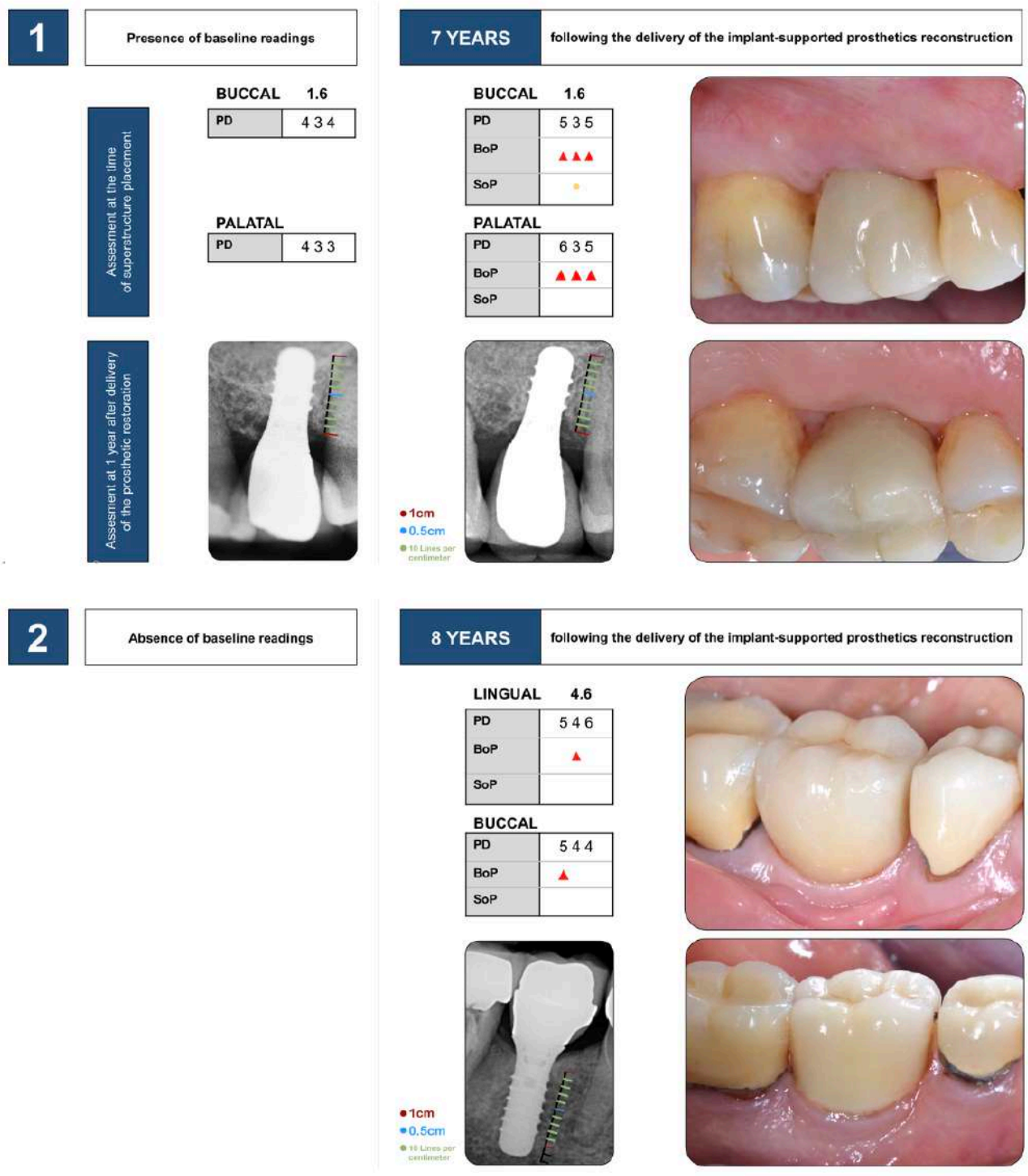


Figure 2. Relative proportions of peri-implant health, peri-implant mucositis and peri-implantitis assigned by examiners for every case along with the case definitions provided by the gold standard examiner

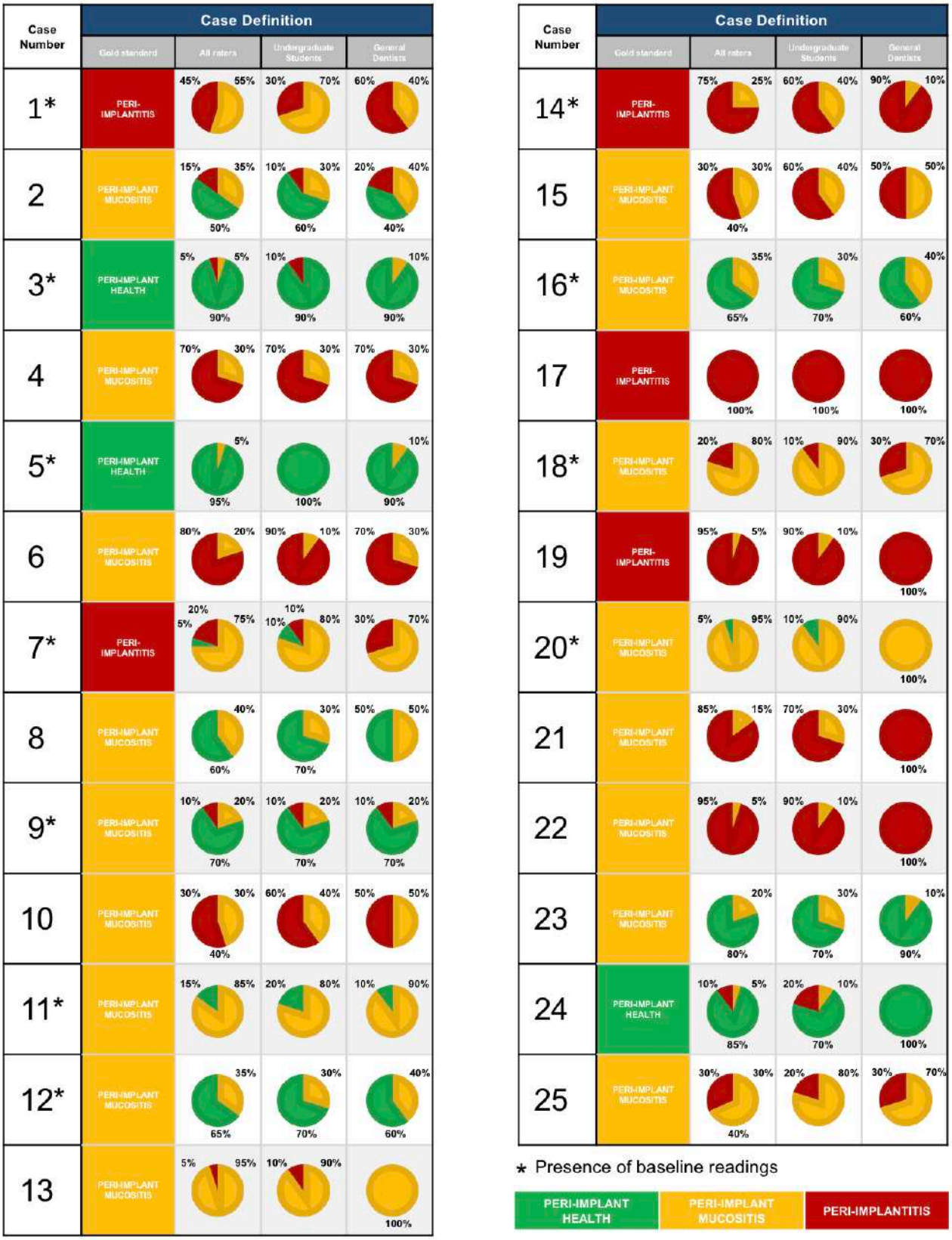


Figure 3. Percentages of slight, fair, moderate, substantial, almost perfect agreements achieved by pairwise comparisons (gold standard vs each examiner)

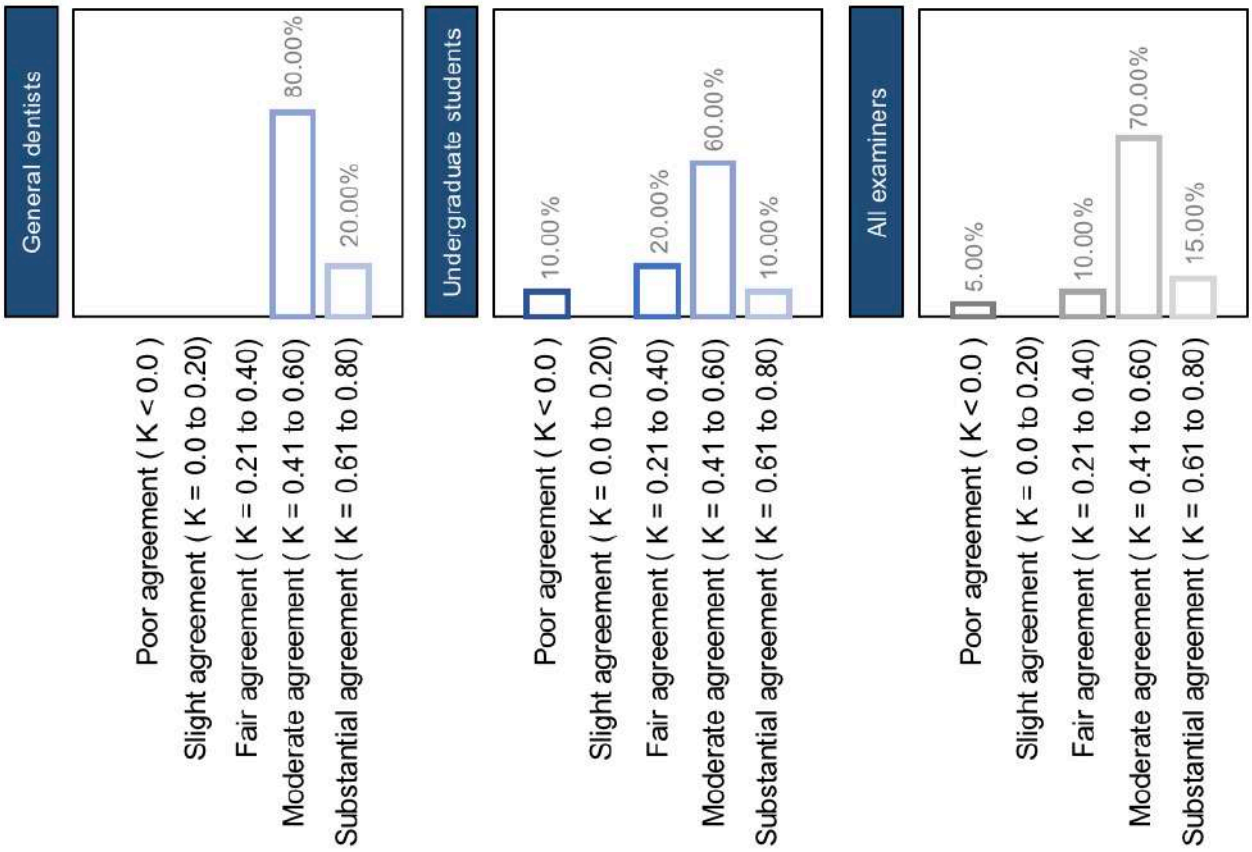
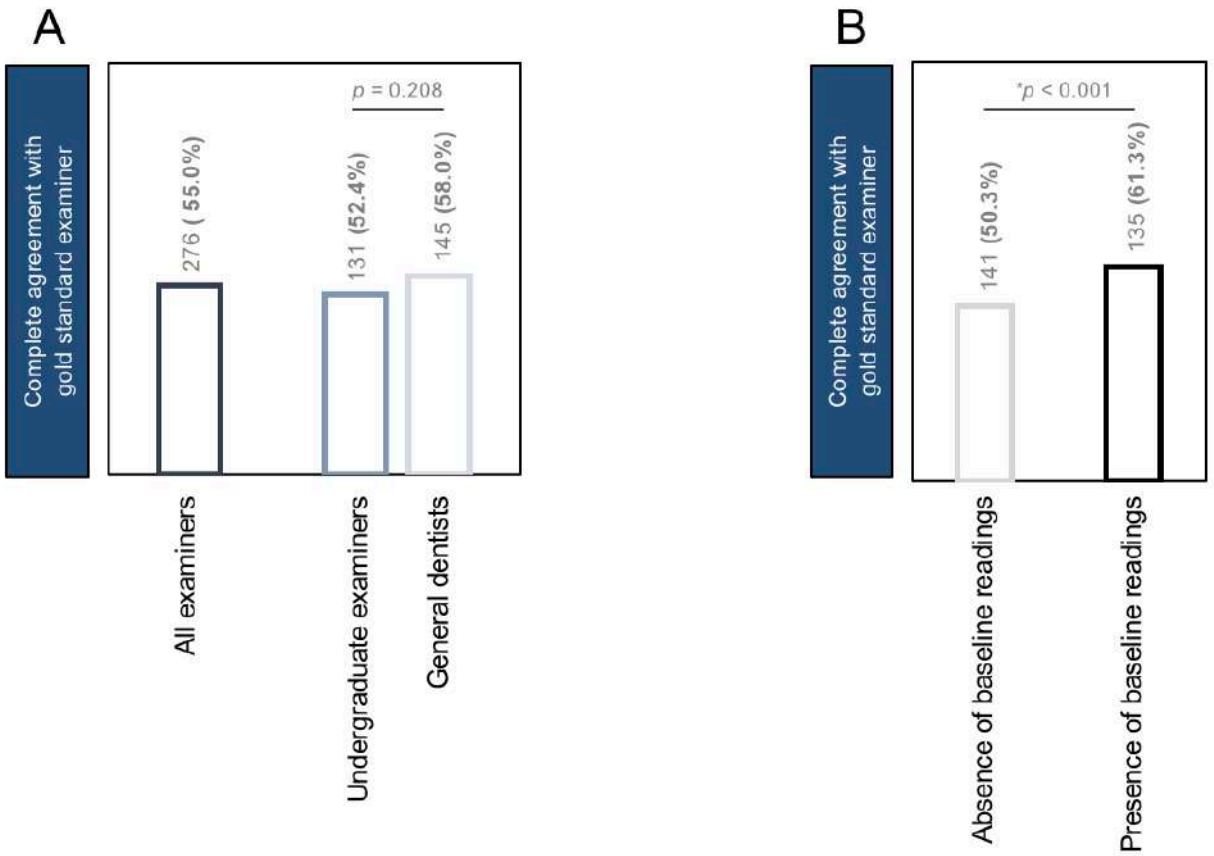


Figure 4. Frequencies and percentages of case definitions consistent with those of the gold standard examiner according to the education and clinical experience of examiners (A) and the presence or absence of baseline readings (B)



†Chi-square test
*, statistically significant

Tables

Table 1. Descriptive characteristics of the twenty-five implant cases

Characteristics	
Years from the delivery of the implant-supported prosthetics reconstruction, mean (SD)	9.2 (± 5.9)
Jaw, N (%)	
Maxilla	15 (60%)
Mandible	10 (40%)
Position, N (%)	
Anterior (canine-canine)	2 (8%)
Posterior	23 (92%)
Retention of supraconstruction, N (%)	
Screw-retained	7 (28%)
Cemented	18 (72%)
Design of supraconstruction, N (%)	
Single unit	19 (76%)
Multi unit	6 (24%)
Base line readings, N (%)	
Presence	11 (44%)
Absence	14 (56%)
Peri-implant health[†], N (%)	
Healthy	3 (12%)
Peri-implant mucositis	16 (64%)
Peri-implantitis	6 (24%)
Presence of bone loss (0.5 mm)[†], N (%)	
No	7 (28%)
Yes	18 (72%)

[†] As evaluated by the gold standard examiner

Table 2. Case definitions assigned by the gold standard examiner and the rationale for each diagnosis

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13
Gold standard definition	P	M	H	M	H	M	P	M	M	M	M	M	P
Justification													
Visible signs of inflammation (red, swollen, soft consistency)	N	N	N	N	N	Y	N	N	N	Y	Y	N	Y
Bleeding on probing	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
Suppuration on probing	Y	N	N	Y	N	Y	N	N	N	N	N	N	Y
Increasing probing pocket depths as compared to measurements obtained at placement of the supra-structure	Y	NA	Y	NA	N	NA	Y	NA	Y	NA	Y	N	NA
Bone loss in relation to the radiographic bone level assessment at 1 year following the delivery of the implant-supported prosthetics reconstruction	N	NA	Y	NA	N	NA	N	NA	Y	NA	N	N	NA
Probing depths ≥6 mm in conjunction with profuse bleeding	NA	N	NA	Y	NA	Y	NA	N	NA	Y	NA	NA	N
Radiographic evidence of bone level ≥3 mm	NA	N	NA	N	NA	N	NA	N	NA	N	NA	NA	N
Radiographic bone level in mm	2	0	1	2	0	2	0	0	1	2	0	1	1
Notes	- No signs of inflammation - BoP+ - SoP+ - PD increase - Bone loss	- BoP+ - PD ≥6 mm - Bone level < 3mm	- No signs of inflammation - PD change in one site - Bone loss 1mm	- No signs of inflammation - Bop+ - SoP+ - PD ≥6 mm - Bone level < 3mm	- No signs of inflammation -No PD increase - No bone loss	- Signs of inflammation – Bop+ - SoP+ - PD ≥6 mm - Bone level < 3mm	- No signs of inflammation -BoP+ - PD increase - No bone loss	- No signs of inflammation - BoP+ .- PD < 6 mm - No bone loss	- No signs of inflammation - BoP+ - 1 mm change in PD at 1 site - Bone loss 1 mm (but projection rx different)	- Signs of inflammation – BoP+ - SoP+ - PD ≥6 mm - Bone level < 3mm	- Signs of inflammation – BoP+ - PD increase - No bone loss	- No signs of inflammation - BoP+ - PD < 6 mm - No bone loss	- Signs of inflammation – BoP+ - SoP+ - PD <6 - Bone level < 3mm

H = peri-implant health, M = mucositis, P = peri-implantitis, Y = Yes, N = No, NA = not available, BoP = bleeding on probing, SoP = suppuration on probing, PD = probing depth

Table 2. (Continue)

	Case 14	Case 15	Case 16	Case 17	Case 18	Case 19	Case 20	Case 21	Case 22	Case 23	Case 24	Case 25
Gold standard definition	P	M	M	P	M	P	M	M	M	M	H	M
Justification												
Visible signs of inflammation (red, swollen, soft consistency)	N	Y	N	Y	N	Y	Y	Y	Y	N	N	Y
Bleeding on probing	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Suppuration on probing	N	N	N	Y	N	Y	Y	Y	Y	N	N	Y
Increasing probing pocket depths as compared to measurements obtained at placement of the supra-structure	Y	NA	N	NA	Y	NA	Y	NA	NA	NA	NA	NA
Bone loss in relation to the radiographic bone level assessment at 1 year following the delivery of the implant-supported prosthetics reconstruction	Y	NA	N	NA	N	NA	N	NA	NA	NA	NA	NA
Probing depths ≥6 mm in conjunction with profuse bleeding	NA	Y	NA	Y	NA	Y	NA	Y	Y	N	N	N
Radiographic evidence of bone level ≥3 mm	NA	N	NA	Y	NA	Y	NA	N	Y	N	N	N
Radiographic bone level in mm	3	1	0	3	1	3	0	1	2	1	0	1
Notes	- No signs of inflammation - BoP+ - PD increase - Bone loss ≥ 3mm	- Signs of inflammation – Bop+ - PD ≥6 mm - Bone level < 3mm	- No signs of inflammation - BoP+ - No PD increase -No bone loss	- Signs of inflammation – Bop+ - SoP+ - PD ≥6 mm -Bone level ≥3 mm	- No signs of inflammation – BoP+ half sites (mesial) -PD increase - -No clear bone loss (baseline radiograph over-projected)	- Signs of inflammation – Bop+ - SoP+ - PD ≥6 mm - Bone level ≥3 mm	- Signs of inflammation – Bop+ - SoP+ - PD increase in 1 site - No bone loss	- Signs of inflammation – Bop+ - SoP+ -PD ≥6 mm - Bone level < 3mm	- Signs of inflammation – Bop+ - SoP+ -PD ≥6 mm - Bone level < 3mm	- No signs of inflammation - BoP+ - PD < 6 mm -No bone loss	- No signs of inflammation - PD < 6 mm -No bone loss	- Signs of inflammation – Bop+ - SoP+ -PD ≥6 mm - Bone level < 3mm

H = peri-implant health, M = mucositis, P = peri-implantitis, Y = Yes, N = No, NA = not available, BoP = bleeding on probing, SoP = suppuration on probing, PD = probing depth

Table 3. Quadratic weighted kappa for pairwise comparisons of each examiner against gold standard examiner (95% confidence interval)

Group	Examiner number	Quadratic weighted kappa	95% CIs (lower, upper bound)
Undergraduate student	1	0.333	0.015, 0.651
	2	0.453	0.123, 0.784
	3	0.395	0.042, 0.747
	4	0.600	0.222, 0.978
	5	0.454	0.077, 0.831
	6	0.566	0.187, 0.945
	7	0.416	0.074, 0.758
	8	-0.007	nc, nc
	9	0.509	0.127, 0.615
	10	0.619	0.210, 1.000
General dentists	1	0.471	0.135, 0.808
	2	0.559	0.170, 0.949
	3	0.590	0.237, 0.943
	4	0.487	0.112, 0.863
	5	0.515	0.137, 0.614
	6	0.605	0.276, 0.935
	7	0.616	0.267, 0.965
	8	0.500	0.157, 0.852
	9	0.513	0.179, 0.846
	10	0.654	0.176, 1.000

Table 4. Fleiss kappa statistics relating to the agreement between the overall group of examiners and between each group of observers

Examiners	Percent overall agreement	Kappa	95% CIs (lower, upper bound)
All	66.74%	0.50	0.47, 0.52
Groups			
General dentists (n=10)	68.71%	0.53	0.48, 0.57
Undergraduate students (n=10)	64.09%	0.46	0.41, 0.50

Chapter Five

Conclusion and implications for further research

The following section highlights the main contributions of the three related research papers. Furthermore, it outlines the critical parameters or components of the case definitions of Periodontitis and Peri-implant Health and Diseases proposed by the 2017 AAP / EFP World Workshop that could lead to misdiagnosis, requiring clarification and more specific education and training. Finally, it proposes indications for future research.

Main findings

The results presented here provided for the first-time information regarding the consistency and accuracy of the clinicians using the case definitions proposed by the 2017 AAP/EFP World Workshop Classification of Periodontitis and Peri-implant Health and Diseases.

Both reproducibility and precision in diagnosis have a considerable impact in clinical and research settings. In clinical setting, it is of paramount importance that patients can be adequately informed about their diagnosis and, as far as periodontitis is concerned, also about the severity of their condition, the identified risk factors and the prognosis. Furthermore, an accurate diagnosis can result in appropriate treatment planning and adequate communication to the patient. The European Federation of Periodontology has provided two distinct guidelines for clinical practice, one for the treatment of Stage I-III Periodontitis and the other for the treatment of Stage IV Periodontitis. A separate guideline for the treatment of Peri-implant diseases will also be published. In research setting, reproducibility and accuracy in diagnosis have an impact in establishing the prevalence of each pathology and influence the results and associations presented in the studies.

The three studies included in this thesis have shown that when clinicians define cases of periodontitis using the AAP / EFP World Workshop 2017 classification, high levels of reproducibility over time are reached. Moreover, moderate agreement across examiners is generally achieved. In addition, clinicians are often accurate in assigning one of the

components of the case definition (particularly the stage) but need more familiarization with the staging and grading system to properly diagnose periodontitis patients (stage + extent + grade). The latter aspect is even more true if the clinicians are not periodontal experts and have not received specific education on classification. In these cases, a substantial advantage could be obtained from being assisted by dedicated software and decision-making algorithms. Regarding peri-implant health and peri-implant diseases case definition assignments, consistency and accuracy were both moderate. The presence of the baseline reading was associated with better results.

Critical aspects of the 2017 AAP / EFP World Workshop case definitions

This part details the parameters or components of the case definitions that could lead to inadequate assignments, identified by the lack of agreement among examiners and the gold standard diagnosis.

- ***Presence or absence of isolated elements in staging and grading***

The application of the 2017 AAP / EFP World Workshop Classification by the examiners sometimes resulted in an overestimation of the staging and grading due to a somewhat too strict interpretation of the presence or absence of isolated elements (e.g. a site with PD> 6 mm is sufficient for move from stage II to stage III). This was even more evident when they defined cases using a software application based on automatic checkbox-based algorithms. In this regard, it has been suggested that upstaging due to complexity factors requires a full evaluation of these parameters by an experienced clinician. Simple identification of the presence / absence of isolated elements in the staging and grading process has not been recommended.

- ***High level assessment of stage***

For the initial staging of a periodontitis case, it is suggested to perform a targeted, high-level assessment of the patient's medical history, radiographs and probing chart to distinguish between stage I or II periodontitis and stage III or IV periodontitis.

The examiners who participated in the present investigations performed well in this task. However, they were better at assigning severe / advanced cases to stage III or IV then early / moderate cases to stage I or II. This was likely due to the greater ease in detecting the data required for staging when they were obvious (i.e., high probing depths and clinical attachment levels and evident radiographic bone loss). Accordingly, the less severe the form of periodontitis, the more difficult it was to correctly diagnose the case.

PERIODONTITIS STAGE		**Stage I**	**Stage II**	**Stage III**	**Stage IV**
Severity	**Interdental CAL at site of greater loss**	1-2 mm	3-4 mm	≥ 5 mm or extending to the middle third of the root	≥ 5 mm or extending to the apical third of the root
	Radiographic bone loss	Coronal third (<15%)	Coronal third (15-33%)	Extending to middle third	Extending to the apical third
	Tooth loss	No tooth loss due to periodontitis		Tooth loss due to periodontitis of ≤ 4 teeth	Tooth loss due to periodontitis of ≥ 5 teeth
Complexity	**Local**	Maximum probing depth ≤4 mm Mostly horizontal bone loss	Maximum probing depth ≤5 mm Mostly horizontal bone loss	In addition to Stage II complexity: Probing depth ≥ 6 mm Vertical bone loss ≥ 3 mm Furcation involvement Class II or III Moderate ridge defect	In addition to Stage III complexity: Need for complex rehabilitation due to: Masticatory disfunction Secondary occlusal trauma (tooth mobility degree ≥ 2 Severe ridge defect Bite collapse, drifting, flaring Less than 20 remaining teeth (10 opposing pairs)
Extent and distribution	**Add to Stage as descriptor**	For each stage, describe extent as localized (<30% of teeth involved), generalized, or molar/incisor pattern			

Table 1. Distinctions between Stages I and II versus Stages III and IV

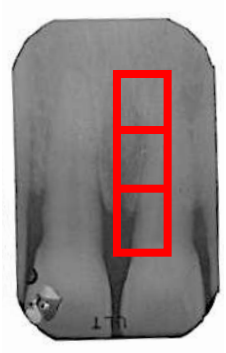


Figure 1. Determination of whether bone loss is likely to be in the most coronal third, the middle third, or the most apical third of the root length

- ***Borderline cases stage I and II***

After proper preliminary evaluation, the chances of correctly distinguishing the case as stage I or II decreased. Furthermore, the accurate definitions of both stage I and II cases were inferior to those of stage III and IV.

The distinction between stage I and II periodontitis is made by focusing on a limited number of parameters: the loss of interproximal clinical attachment (1-2 vs 3-4 mm), probing depths (4 vs 5 mm) and the severity of the bone loss.

The most frequent problem has been how to reliably distinguish between bone loss up to 15% of the root length and bone loss extending between 15% and 33% of the root length. Obviously, the point was not to examine the level of bone loss with a level of accuracy that extended to single percentage points. Instead, the intent was to differentiate between an incipient stage of periodontitis that has barely led to alveolar bone loss, from more substantial bone loss extending within the coronal third of the root length.

In the present research, stage I cases were borderline between gingivitis and periodontitis. They were characterized by an incipient loss of attachment in the presence of early radiographic evidence of resorption of the alveolar bone support (e.g., a break in the integrity of the hard lamina) rather than a pronounced increase in the distance of the CEJ-bone crest. However, the absence of easily discernible bone loss does not preclude the presence of frank periodontitis of incipient severity. This is exactly why the diagnosis of periodontitis is based on attachment loss rather than bone loss, which is certainly more

widely evaluated; the use of bone loss as the main criterion would result in a significant under-detection of incipient periodontitis and an increase in "false negatives".

Although some concerns have been raised regarding the low clinical and radiographic thresholds of the Stage I, they allow early detection and definition of a population of susceptible individuals. This is recognized as a formidable challenge in general dental practice, offering opportunities for prompt intervention and monitoring.

PERIODONTITIS STAGE		**Stage I**	**Stage II**	**Stage III**	**Stage IV**
Severity	**Interdental CAL at site of greater loss**	1-2 mm	3-4 mm	≥ 5 mm or extending to the middle third of the root	≥ 5 mm or extending to the apical third of the root
	Radiographic bone loss	Coronal third (<15%)	Coronal third (15-33%)	Extending to middle third	Extending to the apical third
	Tooth loss	No tooth loss due to periodontitis		Tooth loss due to periodontitis of ≤ 4 teeth	Tooth loss due to periodontitis of ≥ 5 teeth
Complexity	**Local**	Maximum probing depth ≤4 mm Mostly horizontal bone loss	Maximum probing depth ≤5 mm Mostly horizontal bone loss	In addition to Stage II complexity: Probing depth ≥ 6 mm Vertical bone loss ≥ 3 mm Furcation involvement Class II or III Moderate ridge defect	In addition to Stage III complexity: Need for complex rehabilitation due to: Masticatory disfunction Secondary occlusal trauma (tooth mobility degree ≥ 2 Severe ridge defect Bite collapse, drifting, flaring Less than 20 remaining teeth (10 opposing pairs)
Extent and distribution	**Add to Stage as descriptor**	For each stage, describe extent as localized (<30% of teeth involved), generalized, or molar/incisor pattern			

Table 2. Distinctions between Stages I versus II

Figure 1. Stage I periodontitis

Figure 2. Stage II periodontitis

- ***Borderline cases stage III and IV***

Stage III and IV cases were mostly associated with a high level of diagnostic accuracy. However, the ability to discern between borderline stage III and IV cases proved to be the most difficult. In fact, the distinction between these two stages is not based only on the extent of tooth loss attributable to periodontitis (from one to four teeth against five or more teeth) but also on the presence of the various complexity factors.

Borderline cases require clinical judgment and often cannot be classified following simple rigorous algorithmic evaluations outside the parameters of general guidelines. Indeed, the diagnostic process involves a collective assessment of potential complexity factors, rather than a simple "checking of a box" approach of isolated features.

Being able to identify when a borderline Stage III / IV has the potential to become a Stage IV complexity is a key discriminatory factor. First, it should be assessed whether the extent and severity of the patient's periodontitis poses a threat to the survival of individual teeth or rather to the survival of the entire dentition. In particular, the distinction should be based on the subjective assessment of the prognosis of the teeth, which could be influenced by the personal experience of the operator, the training, knowledge and general health orientation of the patient. Secondly, it should be considered whether the overall therapy planned to address the consequences of periodontitis in the particular patient involves extensive and multidisciplinary oral rehabilitation involving the collaboration of multiple experts (in addition to the need for occasional extractions and limited prosthetic reconstructions).

Cases of severe periodontitis without tooth loss due to periodontitis but complicated by flaring or tooth migration and secondary occlusal trauma should challenge the clinician to assign the correct stage. Patient-based clinical judgment, aiming at long-term preservation of natural dentition, guides the assignment of final staging when the case falls into the "gray zone".

PERIODONTITIS STAGE		Stage I	Stage II	Stage III	Stage IV
Severity	**Interdental CAL at site of greater loss**	1-2 mm	3-4 mm	≥ 5 mm or extending to the middle third of the root	≥ 5 mm or extending to the apical third of the root
	Radiographic bone loss	Coronal third (<15%)	Coronal third (15-33%)	Extending to middle third	Extending to the apical third
	Tooth loss	No tooth loss due to periodontitis		Tooth loss due to periodontitis of ≤ 4 teeth	Tooth loss due to periodontitis of ≥ 5 teeth
Complexity	**Local**	Maximum probing depth ≤4 mm Mostly horizontal bone loss	Maximum probing depth ≤5 mm Mostly horizontal bone loss	In addition to Stage II complexity: Probing depth ≥ 6 mm Vertical bone loss ≥ 3 mm Furcation involvement Class II or III Moderate ridge defect	In addition to Stage III complexity: Need for complex rehabilitation due to: Masticatory disfunction Secondary occlusal trauma (tooth mobility degree ≥ 2 Severe ridge defect Bite collapse, drifting, flaring Less than 20 remaining teeth (10 opposing pairs)
Extent and distribution	**Add to Stage as descriptor**	For each stage, describe extent as localized (<30% of teeth involved), generalized, or molar/incisor pattern			

Table 3. Distinctions between Stages III versus IV

Figure 3. Stage III periodontitis

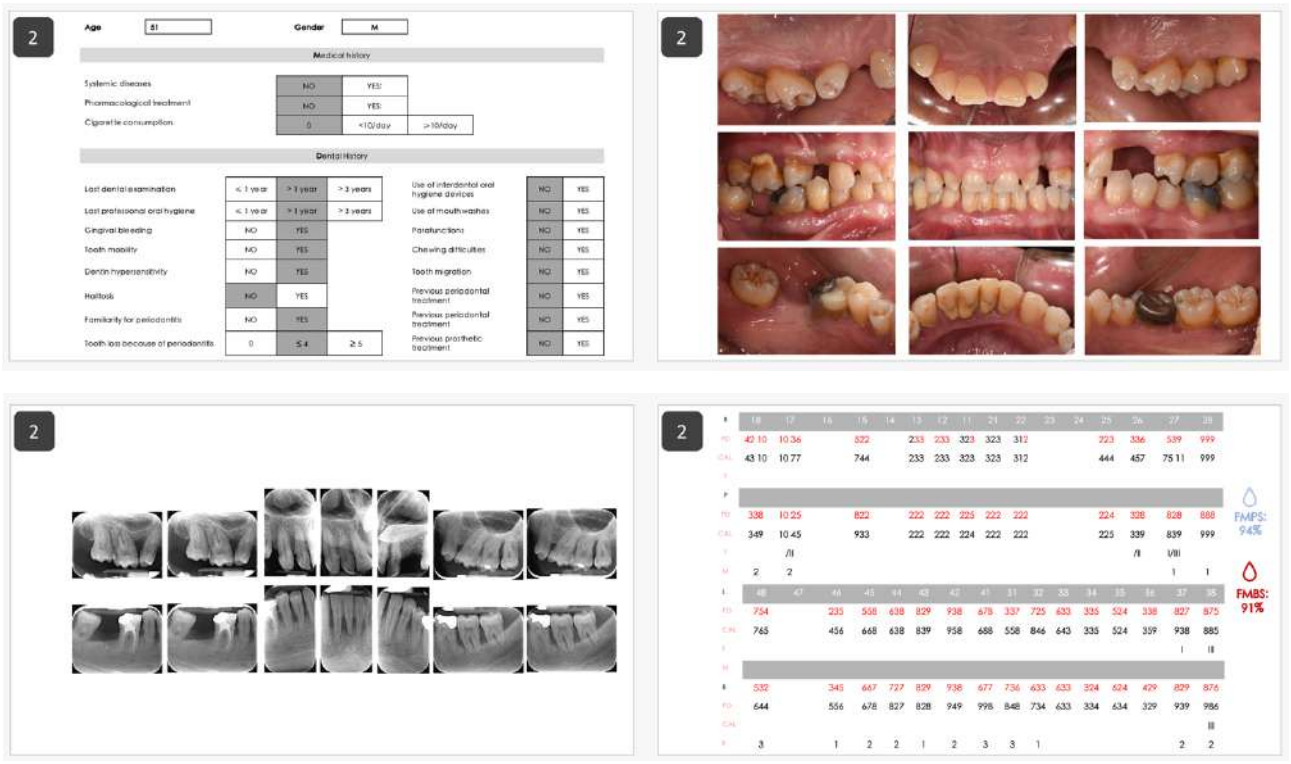


Figure 4. Stage IV periodontitis

- ***Hopeless tooth***

The number of teeth lost because of periodontitis is an important parameter to discriminate between stage I-II and III-IV and between III and IV. In this context, some critical issues were highlighted in the presence of patients with hopeless teeth as it was not clear whether or not they should already be calculated among the teeth lost due to periodontitis.

Teeth with loss of attachment that approximates the apex of the root circumferentially, in combination with a high degree of hypermobility of the teeth (grade III), associated with an obvious negative prognosis, must be calculated among the teeth lost because of periodontitis.

Figure 5. Periapical radiograph showing teeth with loss of attachment that approximates the apex of the root circumferentially, in combination with a high degree of hypermobility of the teeth (grade III)

- ***Missing teeth in the absence of longitudinal data***

It is considered important to point out that the identification of the cause that led to the loss of the teeth is essential to determine the severity of the disease. However, in the investigations covered by this thesis, this information was provided to the examiners without the need of interpretation.

In the absence of previous clinical and radiographic data, it is possible to obtain support for the inclusion of the missing tooth among those lost due to periodontal reason through: 1) asking the patient the cause of an extraction and the symptoms associated with tooth loss (e.g., history of dental hypermobility or extensive caries); 2) assessing the periodontitis severity of clinical attachment level and radiographic bone level on the remaining teeth (especially contralateral). If this cannot be provided and verified, previous tooth loss should not be considered due to periodontitis.

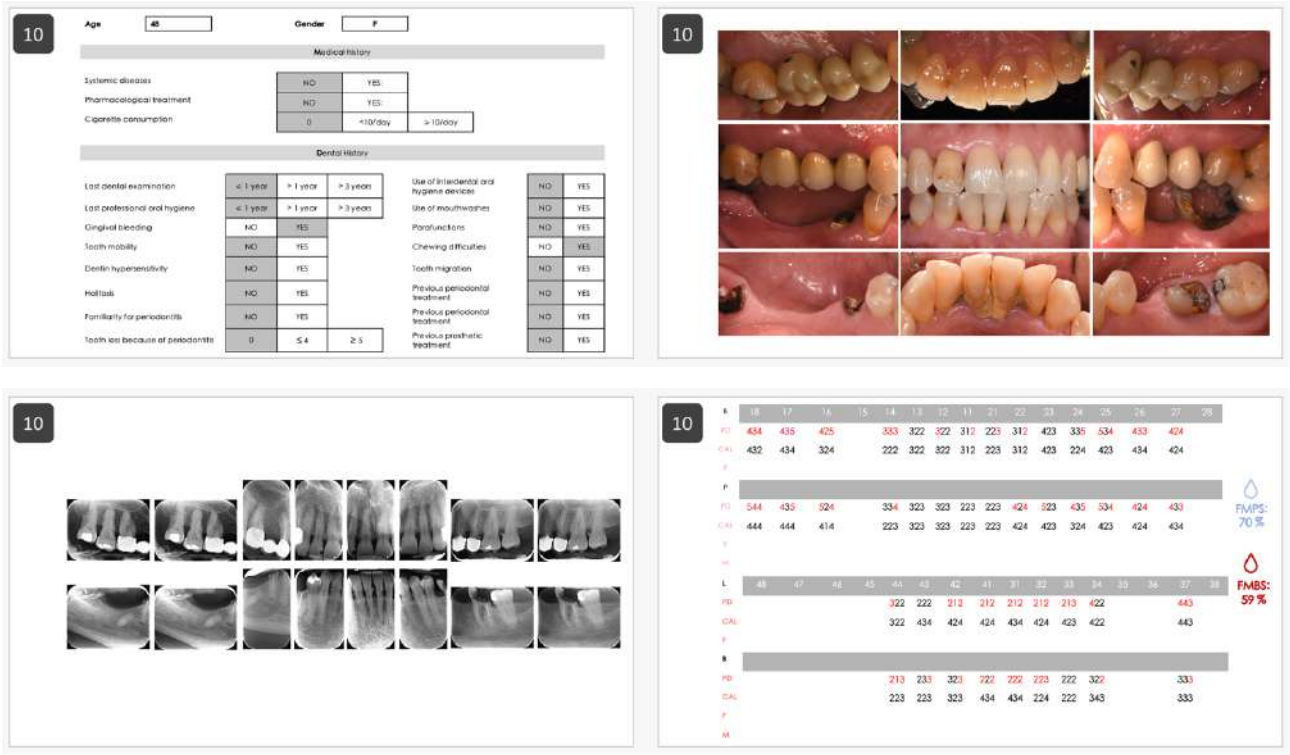


Figure 6. Periodontitis case with missing teeth not due to periodontitis

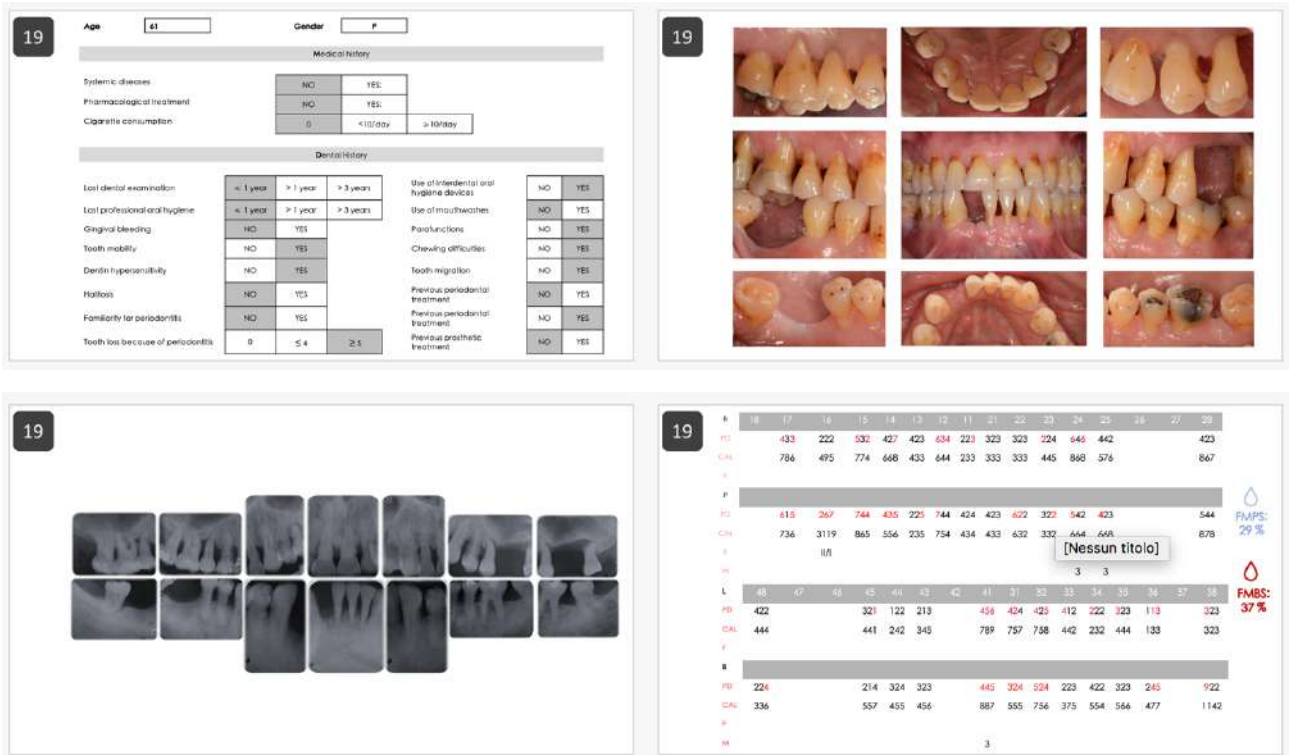


Figure 7. Periodontitis case with missing teeth due to periodontitis

- ***Stage IV on the basis of complexity factors alone***

Only cases of periodontitis with a severity compatible with stage III can be moved to stage IV on the basis of complexity factors, while those with a severity compatible with stage I - II cannot be upshifted.

- ***Bleeding on probing for defining periodontitis stage***

Bleeding on probing is an important clinical parameter for discriminating between health and disease and it has a negative predictive value for periodontitis progression. It is crucial to assess inflammation levels and residual risk after treatment. On the contrary, it is not sufficiently informative neither for the initial evaluation nor to estimate the true level of severity of the disease. Indeed, high levels of bleeding on probing are expected at baseline (when a case is defined) and may provide an initial false representation of case severity.

- ***Extent***

The distribution can be localized (less than 30% of the teeth) or generalized (more than 30% of the teeth) or with a molar-incisor pattern. However, in these researches, one of the most frequent reasons for incorrect extent assignment was to consider the percentage of teeth that contributed to the determination of periodontitis (rather than the percentage of teeth that contributed to the stage of periodontitis).

It has been specified that the extent of periodontitis is defined by the percentage of teeth (non-sites) at the level of severity that defines the stage, i.e. those which present the specific level of severity (CAL / RBL) used to assign the patient's stage.

Although the most severely affected segments of the dentition are those that inevitably define the patient's stage, the clinician is encouraged to expand the description with more relevant information. This fact must be recognized in the "narrative" part of the case description.

As regards the extent of stage IV, it appears that it must be considered by definition to be generalized.

Figure 8. Localized Stage III periodontitis

- ***Indirect evidence of progression using the % bone loss /age ratio***

Most grade definitions that did not agree with the gold standard diagnosis were recorded in cases where grade modifiers were not present and the examiner had to calculate the ratio of percentage bone loss by age. The misdiagnosis was attributed to the incorrect identification of the tooth on which to perform this evaluation and/or to the wrong calculation of the percentage of bone resorption on the designated element.

The assessment of bone loss as a percentage of root length is a rough estimate based on the clinician's interpretation of the most apical location of the alveolar bone support, the location of the CEJ, and the location of the apex of the root.

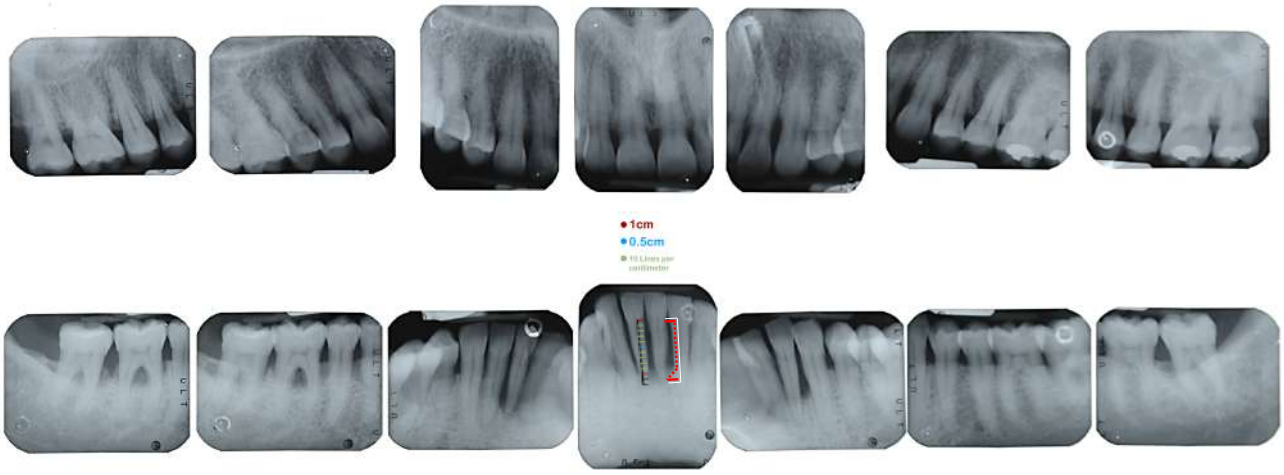


Figure 9. Estimation of radiographic bone loss at site that appears to have most severe destruction

- ***Grade A without longitudinal data***

In non-young patients classified as early (Stage I) or at maximum moderate (Stage II) periodontitis cases, in the absence of modifying factors such as smoking or diabetes, radiographic evidence may suggest a slow rate of progression (Grade A). However, young patients or more severe periodontitis cases will usually have a too high % bone loss / age ratio to be classified as Grade A. Indeed, none of the periodontitis cases included for evaluation in this project have been defined as Grade A by the gold standard diagnosis.

It has been anticipated that an evidence-supported modification to staging and grading classification could refine the thresholds for defining grades A, B, C. From the results of this thesis, it can be assumed that the threshold for the % bone loss / age ratio of grade A could be raised (e.g., from 0.25 to 0.5).

- ***Biofilm deposits for defining periodontitis grade***

The determination of biofilm deposits in relation to periodontal destruction was one of the main characteristics to be considered in the previous classification of periodontitis.

In the current classification system, biofilm deposits should be considered to describe the case phenotype when defining the grading. Case phenotype is relevant when assigning grade through indirect evidence of progression, in absence longitudinal data to determine radiographic bone loss over 5 years. However, indirect evidence of progression is also based

on % radiographic bone loss / age, which appears to have a far greater weight in grade determination than the amount of plaque deposits.
On the other hand, the amount of biofilm deposits was found to have a higher significance when a software based on automatic checkbox-based algorithms was used. In this case, the role of the plaque was probably weighed more than necessary.

- ***Grade assignment in former smokers and subject consuming electronic cigarettes / heat-not-burn tobacco***

Clinicians were found to be able to correctly assess the grade when modifying factors such as smoking and diabetes were present. However, doubts may have arisen in the presence of former smokers. In fact, the literature supports the existence of a different association between the severity of periodontitis between non-smokers and former smokers. Furthermore, the time since a patient has quit smoking has an influence on the risk of periodontitis. In particular, the more time has elapsed the lower the risk. However, the classification does not seem to provide clear indications on how to interpret such clinical scenarios. It is understood that a patient who has smoked 20 cigarettes per day for 40 years and who has quit smoking for 1 year should be considered like someone who has never smoked (as a non-smoker). Finally, no indication has been given on how to consider individuals consuming e-cigarettes and heat-not-burn tobacco.

- ***Significance of bleeding in the case definition of peri-implantitis***

Adequate reliability and accuracy of bleeding on probing around the implant requires careful calibration. In fact, bleeding at implant sites can be influenced by various factors such as: probing force (0.15 N was suggested for probing around the implant); the type of probe and the technique used (in terms of strength and angulation); quantitative and qualitative aspects of the peri-implant biofilm; modifying factors related to the patient and the site that alter the conditions of the host (women > men , additional year of age, anterior implants > posterior implant and interproximal sites > proximal sites); presence of prosthesis or its overhangs / convex profile that prevent an adequate evaluation of the

bleeding (prosthesis must be removed or adjusted when possible or, if not possible, implants should be evaluated with flexible probes). In the third study included in this thesis, examiners had difficulty discriminating between peri-implant health and mucositis in cases of implants lacking other clinical or radiographic signs except for limited sites with bleeding on probing.

It has been suggested that bleeding is often the result of trauma rather than inflammation, due to the mechanical fragility of the peri-implant tissues. Furthermore, although the presence of bleeding at the implant site is associated with a high negative predictive value and high sensitivity, the number of positive bleeding sites that was found to be the strongest predictor of advanced disease progression ranges from three to four. Moreover, non-dichotomous scales should be recommended to classify bleeding by profusion to improve accuracy in diagnosing inflammatory conditions (e.g., mucositis or peri-implantitis).

Figure 10. Implant case showing sites positive for bleeding on probing, defined as peri-implant mucositis

- ***Significance of probing in the case definition of peri-implantitis***

The value of the PPD measurements depends on various prostheses, implants and operator-related factors.

It has been shown that patients with implants displaying PPD ≥ 6 mm have a higher likelihood of progressive bone loss (odds ratio 4.6).

Probing depth ≥ 6 mm was identified as one of the parameters for defining cases of peri-implantitis in the absence of baseline readings by most examiners. However, it could not reflect the actual health of the implant. In fact, it could overestimate the presence of peri-implant mucositis or peri-implantitis if the mucosal implant tunnel had the same width at

baseline, or it could underestimate them if the insertion of the probe was prevented by the prosthetic design. For these reasons, it was adequately considered by examiners only when combined with bleeding and bone level data.
It has also been demonstrated that each 1 mm increase in PD at implant sites increases the likelihood of a diagnosis of peri-implantitis of 100% (odds ratio 2.0).

Figure 11. Implant case displaying one site with PD = 6 mm in absence of baseline readings, defined as peri-implant mucositis

- ***Peri-implantitis definition in absence of baseline readings***

In the absence of previous clinical and radiographic documentation, AAP / EFP World Workshop 2017 Classification proposed a secondary case definition of peri-implantitis: bleeding on probing and / or suppuration on probing at ≥ 1 site and bone level ≥ 3 mm and probing depth ≥ 6 mm. The sensitivity of this definition has been shown to be low, especially for early / incipient forms. In contrast, a secondary case definition based on the presence of BoP / SoP and bone level ≥ 1 mm appeared to provide the best accurate result. Therefore, reduction of the bone level threshold could be suggested.
Similarly, lower levels of agreement with the reference diagnosis were observed when baseline readings were not available, highlighting the importance of longitudinal data for exact diagnosis. The examiners showed difficulty in discriminating between peri-implant mucositis or peri-implantitis when the implants showed a bone level of 1-2 mm, in the absence of previous radiographs.

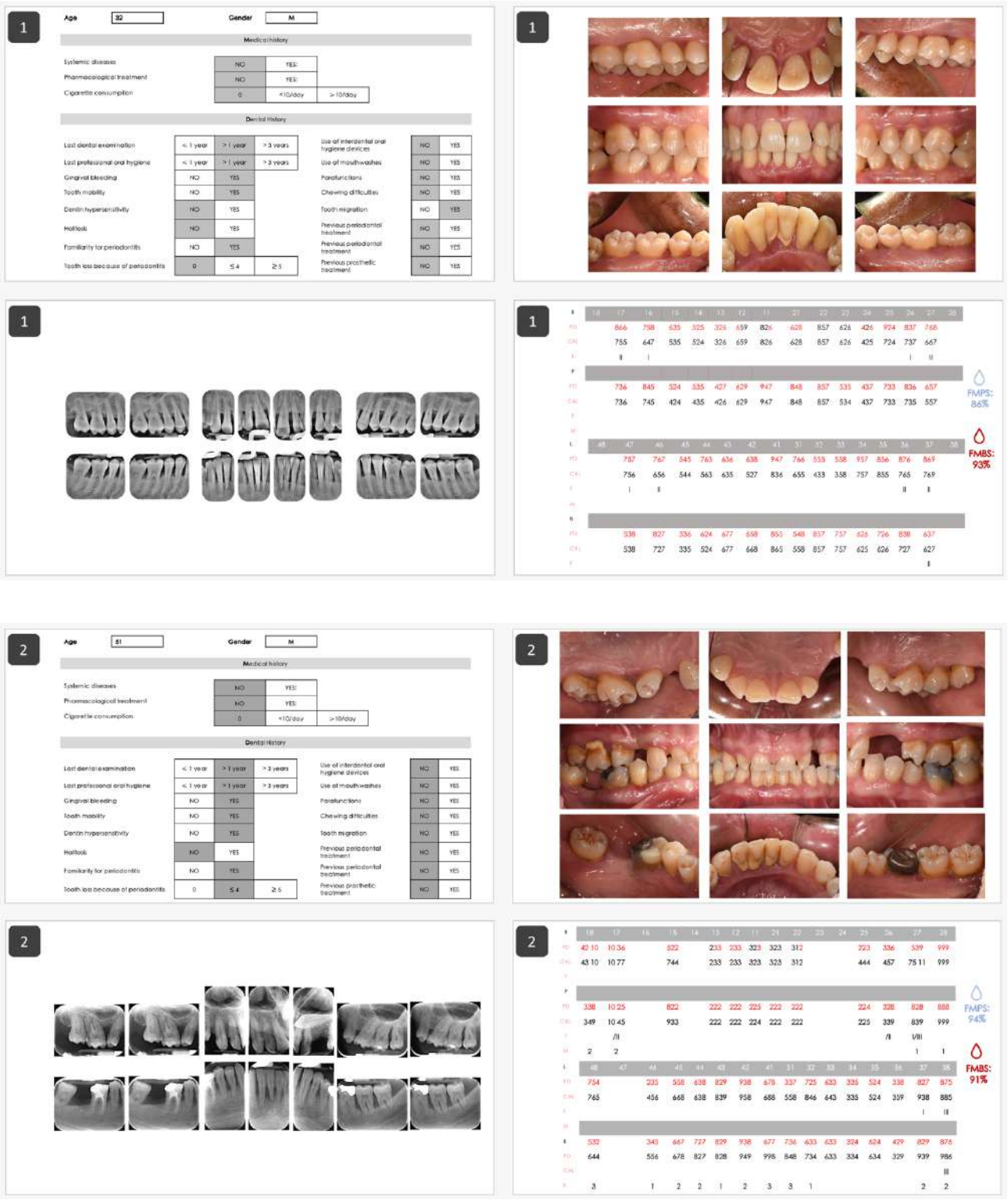
Figure 12. Borderline implant case (peri-implant mucositis vs peri-implantitis) in absence of baseline readings

Future research

Critical issues in clinical application of the AAP / EFP World Workshop 2017 Classification remain to be explored by further investigations in this field. Future studies should be conducted including an higher number of examiners, randomly enrolled among international clinicians with different education and clinical expertise. Moreover, reliability assessment should be performed also on cases showing healthy periodontium and gingivitis. The advantage of using electronic support systems and decision-making algorithms in diagnosing periodontal and peri-implant health and diseases should be further investigated. The assessments should be carried out with and without each of the existing diagnostic supports and they should be directly compared within the same trial. Possibly, it should be also identified the implementation tool that allows to obtain the best results. Finally, it would be useful to conduct studies in which the collection of diagnostic data - unlike what is foreseen in the surveys included in this thesis and in comparable researches - is carried out by the examiners themselves.

Supporting Information

Appendix A. Documentation of the twenty-five cases of periodontitis used for the reliability assessment



3

Age 69 Gender M

Medical history

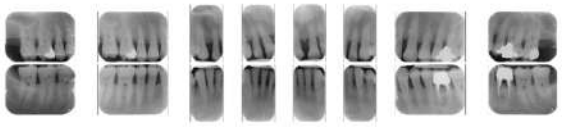
Systemic diseases	NO	YES:	Type 2 Diabetes (HbA1c <7%)
Pharmacological treatment	NO	YES:	
Cigarette consumption	0	<10/day	>10/day

Dental History

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

3

3



3

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD		345	333	435	435	535	547	434	425	535	434	533	736	643	545	
CAL		566	647	657	566	656	668	565	566	665	454	555	736	666	678	
F		I	I											I	II	
P																
PD		556	646	756	535	645	556	434	545	434	534	634	655	433	534	
CAL		667	666	776	766	756	888	766	877	656	554	856	675	564	534	
F		III -	I/-												-/II	
M							1									
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD	866	755	655	545	545	424	444	343	444	444	553	523	554	344	555	556
CAL	866	755	655	545	545	757	777	676	777	777	886	533	554	344	555	556
F																
M														II		
R																
PD	557	564	434	333	223	325	525	523	423	325	411	433	402	444	555	545
CAL	557	556	658	455	365	346	555	573	675	687	732	473	442	444	565	545
F		I	I											II	II	

FMPS: 79%

FMBS: 82%

4

Age 29 Gender F

Medical history

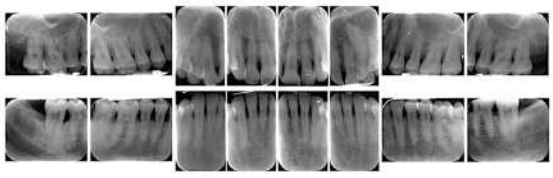
Systemic diseases	NO	YES:	
Pharmacological treatment	NO	YES:	
Cigarette consumption	0	<10/day	>10/day

Dental History

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

4

4



4

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD		545	422	223	222	424	424	424	323	444	224	423	334	434	445	
CAL		454	432	223	242	252	202	232	131	211	031	242	334	444	444	
F																
P																
PD		535	545	334	544	333	333	333	553	333	545	334	534	544	445	
CAL		444	464	333	433	000	001	101	220	000	212	001	223	454	454	
F																
M																
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD	544	344	333	333	333	333	333	333	323	323	323	323	324	445	445	
CAL	213	211	202	202	101	102	212	212	212	212	202	102	203	202	111	
F																
M																
R																
PD	545	333	323	313	313	313	313	313	313	313	323	323	333	334		
CAL	323	201	202	223	202	202	322	222	203	203	102	202	203	201		
F																

FMPS: 23%

FMBS: 11%

5

Age 45 Gender F

Medical history

Systemic diseases	NO	YES	Arterial hypertension
Pharmacological treatment	NO	YES	Diuretics
Cigarette consumption	0	<10/day	>10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO / YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO / YES
Gingival bleeding	NO	YES		Parafunctions	NO / YES
Tooth mobility	NO	YES		Chewing difficulties	NO / YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO / YES
Halitosis	NO	YES		Previous periodontal treatment	NO / YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO / YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO / YES

5

5

5

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD		312		323	333	333	433	322	123	323	328	535	435	626	325	
CAL		423		443	343	343	453	332	133	343	335	455	444	646	334	
P																
PD		323		324	424	322	223	213	322	223	238	324	335	235	325	
CAL		324		424	424	322	223	213	322	223	237	323	334	235	324	
M																
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD		346		324	423	213	333	323	323	324	314	323	432		243	
CAL		347		434	322	435	545	535	434	435	425	434	456		354	
P																
M																
B																
PD		326		343	322	323	333	333	325	525	524	523	422		323	
CAL		438		672	232	234	444	465	544	425	623	442	365		535	

FMPS: 54 %

FMBS: 79 %

6

Age 32 Gender F

Medical history

Systemic diseases	NO	YES	
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	>10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO / YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO / YES
Gingival bleeding	NO	YES		Parafunctions	NO / YES
Tooth mobility	NO	YES		Chewing difficulties	NO / YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO / YES
Halitosis	NO	YES		Previous periodontal treatment	NO / YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO / YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO / YES

6

6

6

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD	334	434		323	323	423	323	323	323	323	323	423	323	324	434	433
CAL	001	201		030	030	100	000	000	000	000	000	100	000	031	102	100
P																
PD	434	434		323	323	323	323	323	323	323	323	323	323	324	434	444
CAL	001	101		000	000	000	000	000	000	000	000	000	000	001	101	100
M																
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD	434	424	333		323	314	313	313	313	313	323	323	323		434	434
CAL	000	101	000		000	020	030	020	020	020	000	000	000		100	100
P																
M																
B	444	433	324		334	334	323	323	323	323	323	323	323		323	334
PD	011	200	050		061	050	000	000	000	000	000	050	050		040	000
CAL																

FMPS: 32%

FMBS: 42%

7

Age 37 Gender F

Medical history

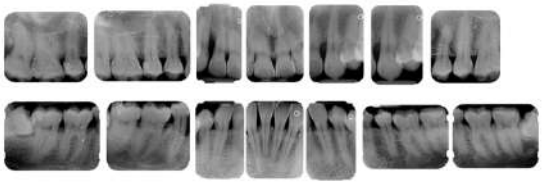
Systemic diseases	NO	YES	
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	>10/day

Dental History

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

7

7



7

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD	223	323	322	323	328	522	223		222	225	534	323	322	333		
CAL	132	232	201	202	308	501	102		202	204	401	202	301	313		
F																
P																
PD	323	323	323	322	326	422	222		222	224	532	333	323	333		
CAL	342	333	212	201	204	201	202		202	212	312	212	212	222		
F																
M																
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD	433	437	556	323	222	322	222	223	222	223	213	332	533	334		
CAL	424	336	355	212	232	332	232	233	232	233	212	332	422	333		
F																
M																
R																
PD	433	437	339	323	323	312	212	213	313	323	312	303	423	324		
CAL	445	545	317	202	313	302	202	202	303	303	201	203	202	100		
F																

FMPS: 31 %

FMBS: 80 %

8

Age 82 Gender F

Medical history

Systemic diseases	NO	YES	Type 2 Diabetes (HbA1c ≥7%) Hypercholesterolemia
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	>10/day

Dental History

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

8

8

8

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD	324	424	525	325	513	213	213		313	314	323	323	323	324	333	
CAL	314	414	524	424	413	203	103		313	314	522	322	212	224	333	
F																
P																
PD	324	423	323	324	523	324	323		323	325	322	423	333	423	333	
CAL	334	443	212	212	423	314	212		323	324	322	443	333	323	333	
F																
M																
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD	345	579	333	424	333	333	885	558	883	323	323	435	536	534		
CAL	344	488	313	414	323	345	10 97	779	995	533	312	314	425	424		
F		2											1	1		
M						1	2	2	2							
R																
PD	369	533	325	464	424	424	62 10	436	633	333	323	323	333	888		
CAL	369	533	325	484	424	424	62 10	436	634	433	323	323	333	888		
F	2	1												2		

FMPS: 65%

FMBS: 90%

9

Age 44 Gender M

Medical history

Systemic diseases	NO	YES	
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	>10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

9

9

9

B	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD		666	756	524	426	724	645	525	623	324	515	444	434	646	765	
CAL		665	665	423	325	624	434	424	523	324	514	353	333	575	665	
F																
P																
PD		766	446	545	534	535	425	636	646	534	535	666	646	646	666	
CAL		777	456	545	534	534	424	535	545	534	535	666	646	656	666	
F																
M																
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD		434	466	445	533	333	333	534	434	333	333	323	335	435	636	
CAL		434	466	334	422	222	343	544	444	343	333	323	224	444	536	
F																
B																
PD		623	425	323	333	333	336	626	626	334	533	424	324	725	646	
CAL		623	424	232	242	222	334	415	514	224	422	343	324	635	646	
F																
M																

FMPS: 77%

FMBS: 80%

10

Age 45 Gender F

Medical history

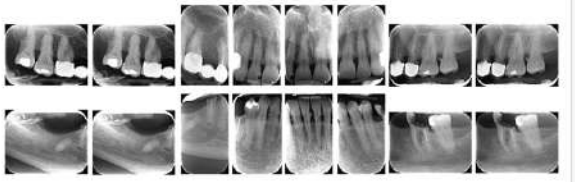
Systemic diseases	NO	YES	
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	>10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

10

10



10

B	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD	434	435	425		333	322	322	312	223	312	423	335	534	433	424	
CAL	432	434	324		222	322	322	312	223	312	423	224	423	434	424	
F																
P																
PD	544	435	524		334	323	323	223	223	424	523	435	534	424	433	
CAL	444	444	414		223	323	323	223	223	424	423	324	423	424	434	
F																
M																
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD					322	222	212	212	212	212	213	422			443	
CAL					322	434	424	424	434	424	423	422			443	
F																
B																
PD					213	233	323	222	222	223	222	322			333	
CAL					223	223	323	434	434	224	222	343			333	
F																
M																

FMPS: 70 %

FMBS: 59 %

11

Age 64 Gender M

Medical history

Systemic diseases	NO	YES:	Myocardial infarction (3 years before)
Pharmacological treatment	NO	YES:	Oral Anticoagulant Therapy
Cigarette consumption	0	<10/day	>10/day

Dental History

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

11

11

11

B	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD		535	525	435	437	333	324	435	543	433	323	423	534		533	333
CAL		757	747	546	458	553	344	445	543	553	353	422	444		655	455
F																
P																
PD		444	334	325	326	323	224	435	523	333	323	433	533		333	334
CAL		455	565	444	346	323	234	435	543	333	333	433	544		464	454
F		/II	II/I													
M		I														I
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD				336	544	323	323	323	323	222	323	323	323	423		
CAL				877	654	333	333	333	333	232	323	333	333	444		
F														I		
B																
PD				546	455	333	333	222	223	323	323	323	323	322		
CAL				998	595	333	333	222	233	323	323	343	343	454		
F														I		
M																

FMPS: 65%

FMBS: 59%

12

Age 51 Gender F

Medical history

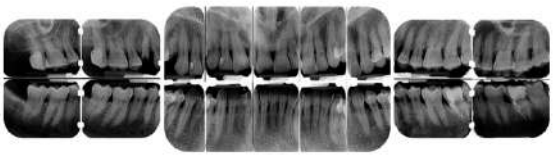
Systemic diseases	NO	YES:	Gastritis
Pharmacological treatment	NO	YES:	Proton-pump inhibitor
Cigarette consumption	0	<10/day	>10/day

Dental History

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

12

12



12

B	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD		332	213	222		222	333	323	323	323	323	322	222	332	335	444
CAL		453	334	343		333	444	443	344	444	333	442	233	444	443	342
F																
P																
PD		533	223	332		223	333	223	212	212	222	223	223	324	335	545
CAL		433	223	333		323	333	223	212	212	222	223	222	334	333	333
F																
M																
L	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD		433	333	433	222	222	222	212	212	232	333	323	326	435	535	
CAL		332	222	322	121	222	222	223	322	232	342	212	214	324	423	
F																
M																
B																
PD		533	222	213	213	233	322	222	212	222	212	212	212	223	434	
CAL		433	242	223	233	344	443	333	323	343	333	242	232	233	333	

FMPS: 45 %

FMBS: 53 %

13

Age 36 Gender F

Medical history

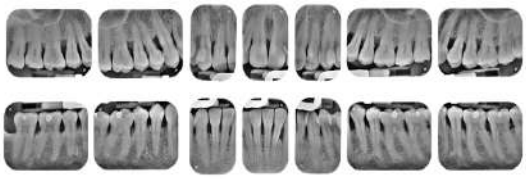
Systemic diseases	NO	YES	
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	>10/day

Dental History

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

13

13



13

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD	444	736	638	835	557	725	622	325	323	333	326	736	538	637	637	834
CAL	444	756	647	734	556	625	622	335	323	333	336	736	547	556	537	834
F																
P																
PD	636	635	537	636	637	743	623	225	333	333	326	735	535	636	637	743
CAL	635	535	537	636	637	743	623	225	333	333	326	735	535	636	637	743
I		II/I	II/I											I/II	I/II	
M																

FMPS: 81%

	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD		336	537	323	323	323	323	323	423	326	646	323	323	335	637	556
CAL		325	516	323	323	323	323	323	423	326	646	323	323	334	636	556
F																
M								I	I							

FMBS: 74%

B																
PD		336	635	433	333	333	423	423	423	346	436	323	325	633	698	586
CAL		336	534	323	332	233	412	333	413	346	556	513	214	522	547	586
F																

14

Age 74 Gender F

Medical history

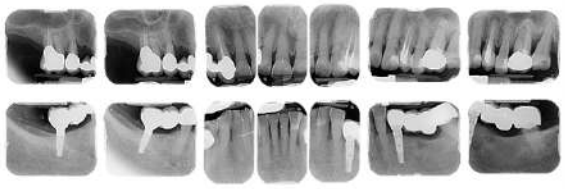
Systemic diseases	NO	YES	
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	>10/day

Dental History

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

14

14



14

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
B																
PD			324	346		523	323	323	323	222	225	523	323	425	835	
CAL			434	456		645	434	333	233	222	235	523	545	637	977	
F																
P																
PD			323	335		323	323	323	222	212	324	423	323	543	545	
CAL			333	345		445	323	333	232	212	324	423	434	697	856	
I																
M																

FMPS: 88%

	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
L																
PD		324		323	323	323	322	222	223	334	423	323			325	
CAL		111		423	534	544	555	445	556	545	344				325	
F																
B																
PD	[Nessun titolo]		323	324	525	423	323	322	226	524	323				423	
CAL		011	323	433	436	624	434	434	446	635	523				423	
F																
M																

FMBS: 66%

15

Age 33 Gender M

Medical history

Systemic diseases	NO	YES:
Pharmacological treatment	NO	YES:
Cigarette consumption	0	<10/day / >10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO / YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO / YES
Gingival bleeding	NO	YES		Parafunctions	NO / YES
Tooth mobility	NO	YES		Chewing difficulties	NO / YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO / YES
Halitosis	NO	YES		Previous periodontal treatment	NO / YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO / YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO / YES

15

15

15

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD	434	424	424	423	323	323	322	222	222	222	323	423	423	224	232	224
CAL	112	202	101	000	000	000	000	000	000	000	000	000	000	102	202	201
F																
P																
PD	434	424	424	423	323	323	324	213	323	323	323	323	323	424	424	424
CAL	202	201	111	000	000	000	000	000	000	000	000	000	000	101	201	101
F																
M																

FMPS: 58%

	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
L																
PD	434	424	424	424	423	323	323	323	323	323	323	323	324	425	434	434
CAL	202	202	201	000	000	000	000	000	000	000	000	000	000	102	202	101
F																
M																

FMBS: 57%

PD	434	424	424	423	324	423	423	323	324	323	323	323	324	424	424	524
CAL	101	101	201	100	000	000	000	000	000	000	000	000	001	102	202	101
F																
M																

16

Age 47 Gender F

Medical history

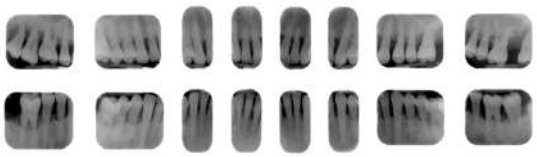
Systemic diseases	NO	YES:
Pharmacological treatment	NO	YES:
Cigarette consumption	0	<10/day / >10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO / YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO / YES
Gingival bleeding	NO	YES		Parafunctions	NO / YES
Tooth mobility	NO	YES		Chewing difficulties	NO / YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO / YES
Halitosis	NO	YES		Previous periodontal treatment	NO / YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO / YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO / YES

16

16



16

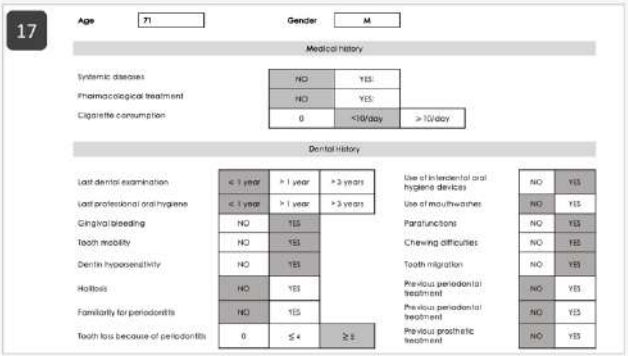
	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD	434	434	627	726	526	726	626	525	524	426	627	628	626	627		979
CAL	989	998	847	745	445	535	626	546	746	626	748	648	646	648		989
F			I											I		
P																
PD	434	435	667	626	737	735	635	535	535	546	456	556	525	424		789
CAL	989	999	788	737	737	634	535	535	666	546	466	566	535	465		998
F		II/II	II/II											II/I		
M	3	3	1					I	2	1				2		

FMPS: 79%

	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
L																
PD			648	866	676	625	522	213	224	434	634	557	868	11 77	776	
CAL			757	755	565	524	532	223	234	444	644	547	868	11 87	786	
F			II											II	II	
M			1				1	2	2	1				2	2	

FMBS: 50%

PD			225	525	625	626	735	525	626	536	726	536	628	11 39	779	
CAL			435	535	635	626	735	536	636	536	726	546	638	11 49	779	
F			I											I	I	


17

Age 71 Gender M

Medical history

Systemic diseases	NO	YES	
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	>10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES


17

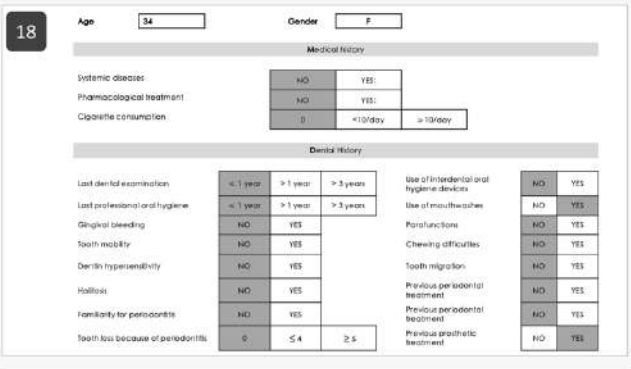

17


17

[Nessun titolo]

FMPS: 45 %

FMBS: 49 %


18

Age 34 Gender F

Medical history

Systemic diseases	NO	YES	
Pharmacological treatment	NO	YES	
Cigarette consumption	0	<10/day	≥ 10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

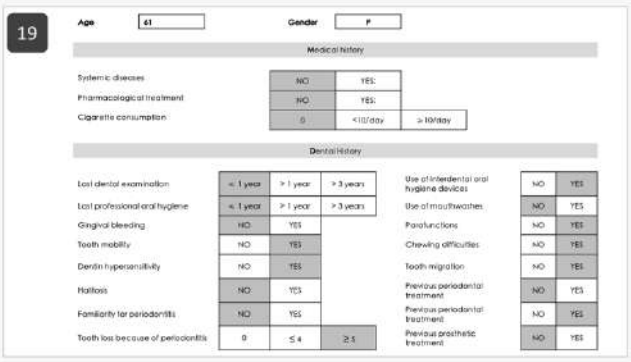

18


18


18

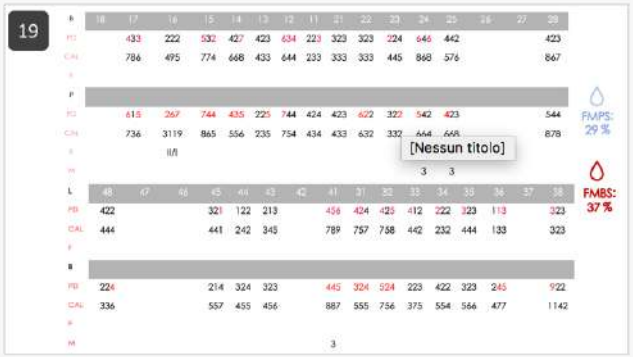
FMPS: 68%

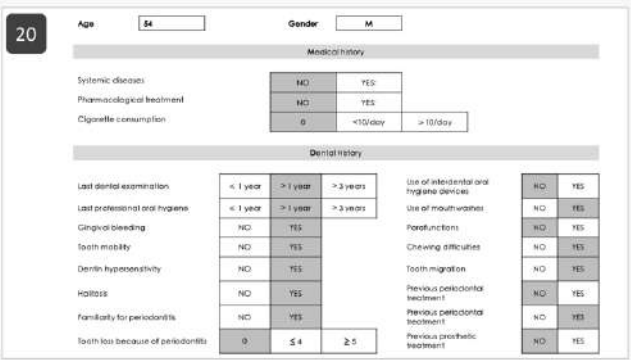
FMBS: 58%


19
Age
61
Gender
F
Medical history
Systemic diseases
NO
YES
Pharmacological treatment
NO
YES
Cigarette consumption
0
<10/day
>10/day
Dental history
Last dental examination
< 1 year
> 1 year
> 3 years
Last professional oral hygiene
< 1 year
> 1 year
> 3 years
Gingival bleeding
NO
YES
Tooth mobility
NO
YES
Dentin hypersensitivity
NO
YES
Halitosis
NO
YES
Familiarity for periodontitis
NO
YES
Tooth loss because of periodontitis
0
≤ 4
≥ 5
Use of interdental oral hygiene devices
NO
YES
Use of mouthwashes
NO
YES
Parafunctions
NO
YES
Chewing difficulties
NO
YES
Tooth migration
NO
YES
Previous periodontal treatment
NO
YES
Previous periodontal treatment
NO
YES
Previous prosthetic treatment
NO
YES

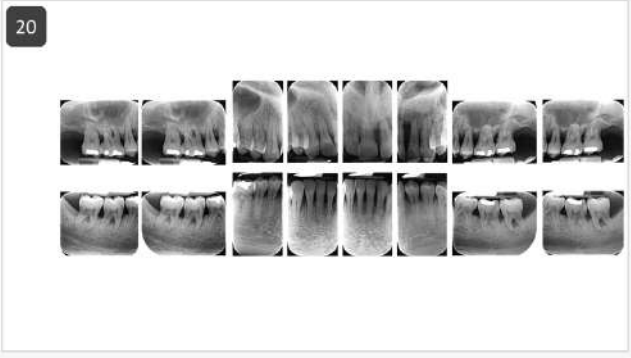

19

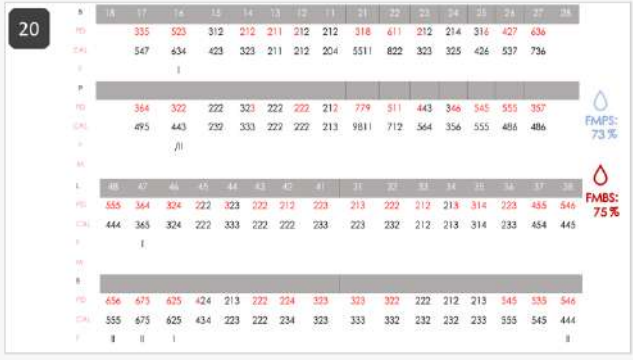

19


19
FMPS: 29 %
FMBS: 37 %
[Nessun titolo]


20
Age
54
Gender
M
Medical history
Systemic diseases
NO
YES
Pharmacological treatment
NO
YES
Cigarette consumption
0
<10/day
>10/day
Dental history
Last dental examination
< 1 year
> 1 year
> 3 years
Last professional oral hygiene
< 1 year
> 1 year
> 3 years
Gingival bleeding
NO
YES
Tooth mobility
NO
YES
Dentin hypersensitivity
NO
YES
Halitosis
NO
YES
Familiarity for periodontitis
NO
YES
Tooth loss because of periodontitis
0
≤ 4
≥ 5
Use of interdental oral hygiene devices
NO
YES
Use of mouthwashes
NO
YES
Parafunctions
NO
YES
Chewing difficulties
NO
YES
Tooth migration
NO
YES
Previous periodontal treatment
NO
YES
Previous periodontal treatment
NO
YES
Previous prosthetic treatment
NO
YES


20


20


20
FMPS: 73 %
FMBS: 75 %

21

Age 40 Gender M

Medical history

Systemic diseases	NO	YES
Pharmacological treatment	NO	YES
Cigarette consumption	0	<10/day	≥ 10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

21

21

21

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD	858	939	936	735	534	335	536	633	324	323	323	323	325	547	748	757
CAL	858	839	936	735	534	335	525	533	324	323	323	323	324	447	748	757
F																
P																
PD	858	1057	736	424	424	423	324	423	233	323	325	525	525	637	759	757
CAL	858	957	736	424	424	423	324	423	233	323	325	525	525	637	759	757
F																
M																

FMPS: 96%

	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD	747	756	635	525	434	423	323	323	323	323	335	535	425	436	624	
CAL	747	756	635	525	434	423	323	323	323	323	335	535	425	436	624	
F																
M								1	1							
II																
PD	747	735	534	424	423	325	424	423	323	327	624	424	425	436	623	
CAL	647	735	534	424	423	325	424	435	533	327	624	424	425	436	623	
F																

FMBS: 100%

22

Age 56 Gender F

Medical history

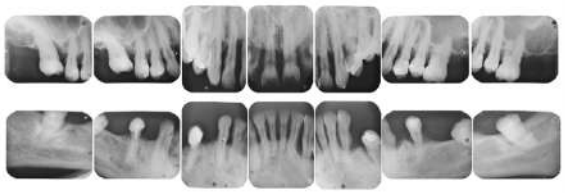
Systemic diseases	NO	YES	Arterial hypertension and depression
Pharmacological treatment	NO	YES	ACE inhibitors and antidepressants
Cigarette consumption	0	<10/day	≥ 10/day

Dental history

Last dental examination	< 1 year	> 1 year	> 3 years	Use of interdental oral hygiene devices	NO	YES
Last professional oral hygiene	< 1 year	> 1 year	> 3 years	Use of mouthwashes	NO	YES
Gingival bleeding	NO	YES		Parafunctions	NO	YES
Tooth mobility	NO	YES		Chewing difficulties	NO	YES
Dentin hypersensitivity	NO	YES		Tooth migration	NO	YES
Halitosis	NO	YES		Previous periodontal treatment	NO	YES
Familiarity for periodontitis	NO	YES		Previous periodontal treatment	NO	YES
Tooth loss because of periodontitis	0	≤ 4	≥ 5	Previous prosthetic treatment	NO	YES

22

22



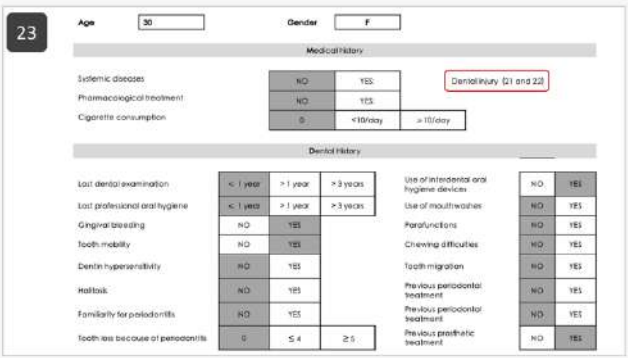
22

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PD		659		516	615	726	758	616	615	616	416	627	416	516		
CAL		656		724	523	526	6510	819	817	817	416	535	213	538		
F							1	1	1	1						
P																
PD		618		414	414	646	637	646	624	445	224	426	414	615		
CAL		736		424	225	646	748	868	825	556	226	534	213	638		
F		II/I												II/I		
M		1												1		

FMPS: 80 %

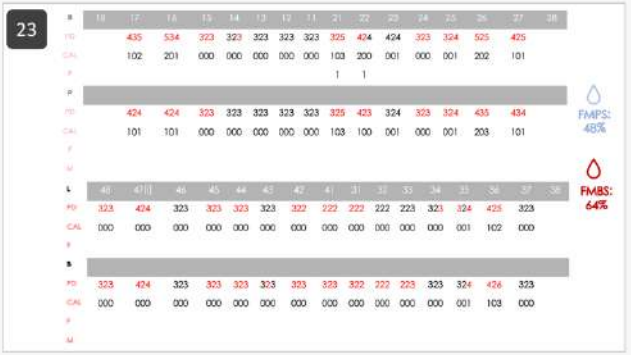
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
PD	757			444		224	412	224	453	215	979		766		1146	
CAL	565			113		215	514	447	654	415	9810		567		754	
F				V/T -												
M	1							1	1				1		3	
II																
PD	757			323		213	412	323	322	223	329		816		646	
CAL	524			333		215	514	547	733	413	4311		637		316	
F																

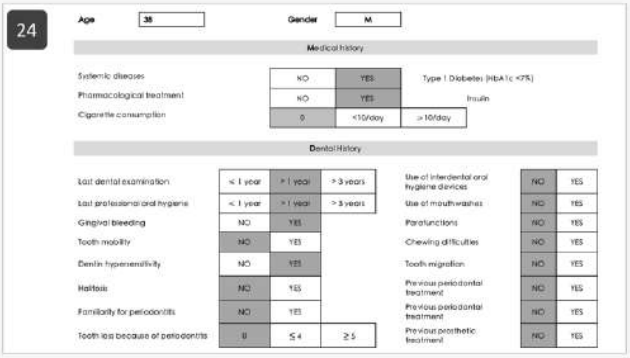
FMBS: 71 %


23
Age 30
Gender F
Medical history
Systemic diseases NO YES
Pharmacological treatment NO YES
Cigarette consumption 0 <10/day >10/day
Dental injury (21 and 22)
Dental history
Last dental examination < 1 year > 1 year > 3 years
Last professional oral hygiene < 1 year > 1 year > 3 years
Gingival bleeding NO YES
Tooth mobility NO YES
Dentin hypersensitivity NO YES
Halitosis NO YES
Familiarity for periodontitis NO YES
Tooth loss because of periodontitis 0 ≤ 4 ≥ 5
Use of interdental oral hygiene devices NO YES
Use of mouthwashes NO YES
Parafunctions NO YES
Chewing difficulties NO YES
Tooth migration NO YES
Previous periodontal treatment NO YES
Previous periodontal treatment NO YES
Previous prosthetic treatment NO YES


23

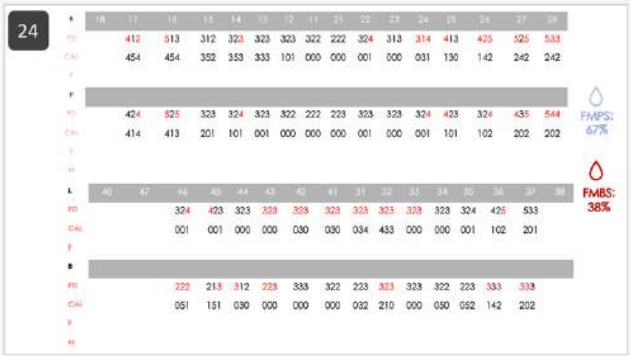

23

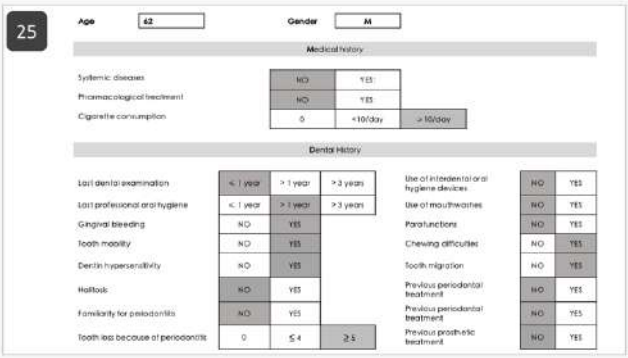

23
FMPS: 48%
FMBS: 64%


24
Age 38
Gender M
Medical history
Systemic diseases NO YES Type 1 Diabetes (HbA1c <7%)
Pharmacological treatment NO YES Insulin
Cigarette consumption 0 <10/day >10/day
Dental history
Last dental examination < 1 year > 1 year > 3 years
Last professional oral hygiene < 1 year > 1 year > 3 years
Gingival bleeding NO YES
Tooth mobility NO YES
Dentin hypersensitivity NO YES
Halitosis NO YES
Familiarity for periodontitis NO YES
Tooth loss because of periodontitis 0 ≤ 4 ≥ 5
Use of interdental oral hygiene devices NO YES
Use of mouthwashes NO YES
Parafunctions NO YES
Chewing difficulties NO YES
Tooth migration NO YES
Previous periodontal treatment NO YES
Previous periodontal treatment NO YES
Previous prosthetic treatment NO YES

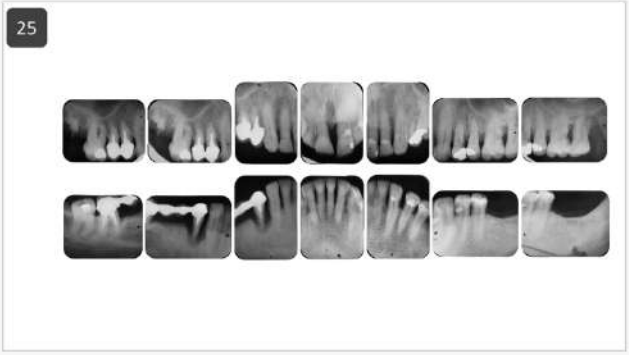

24


24


24
FMPS: 67%
FMBS: 38%

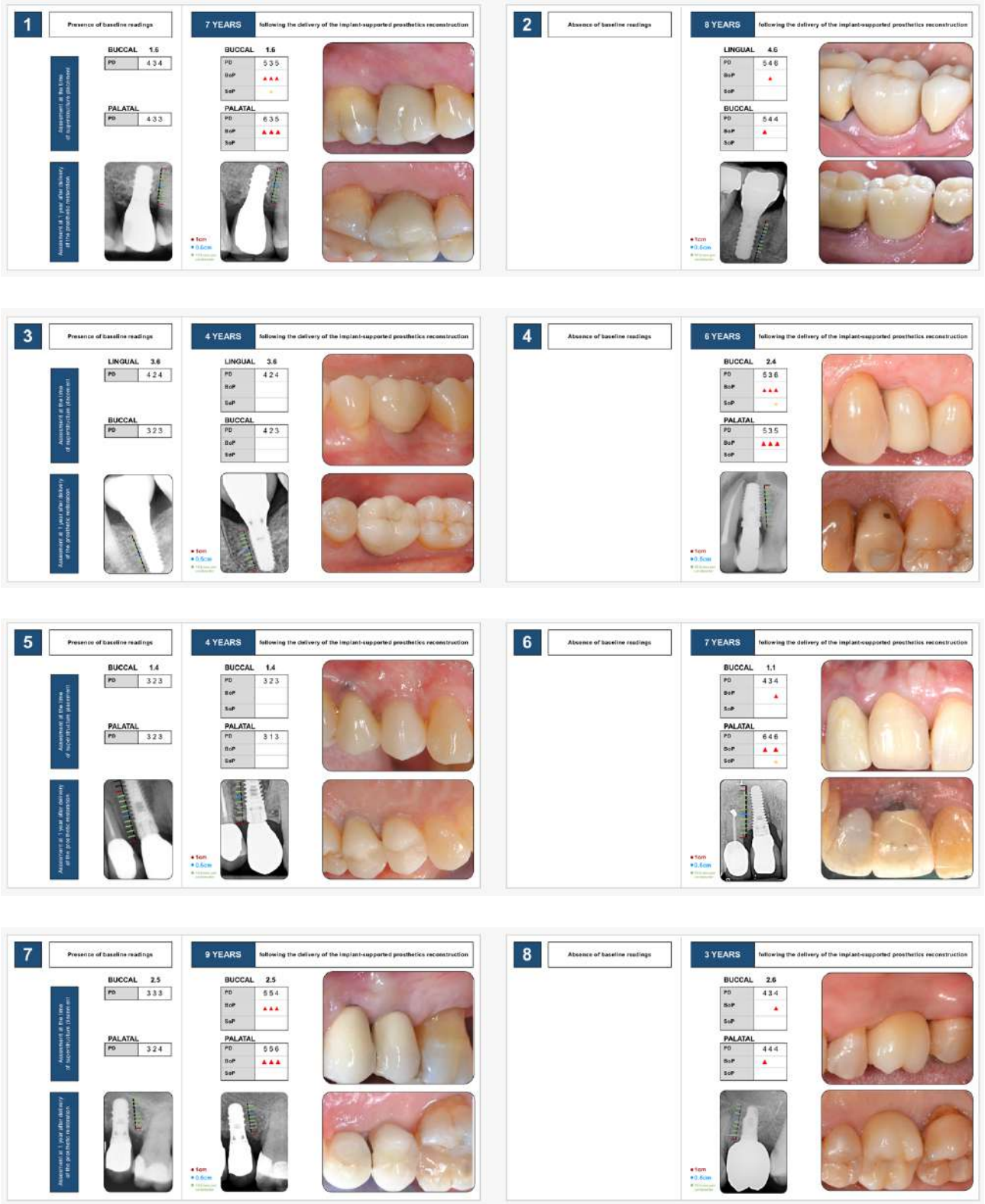

25
Age
62
Gender
M
Medical history
Systemic diseases
NO
YES
Pharmacological treatment
NO
YES
Cigarette consumption
0
<10/day
> 10/day
Dental History
Last dental examination
< 1 year
> 1 year
> 3 years
Last professional oral hygiene
< 1 year
> 1 year
> 3 years
Gingival bleeding
NO
YES
Tooth mobility
NO
YES
Dentin hypersensitivity
NO
YES
Halitosis
NO
YES
Familiarity for periodontitis
NO
YES
Tooth loss because of periodontitis
0
≤ 4
≥ 5
Use of interdental oral hygiene devices
NO
YES
Use of mouthwashes
NO
YES
Parafunctions
NO
YES
Chewing difficulties
NO
YES
Tooth migration
NO
YES
Previous periodontal treatment
NO
YES
Previous periodontal treatment
NO
YES
Previous prosthetic treatment
NO
YES


25

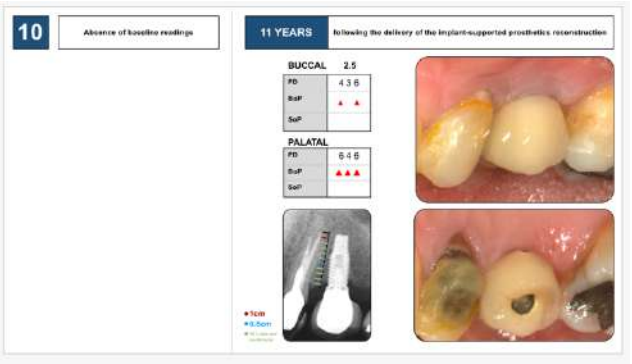

25


25
FMPS: 48 %
FMBS: 25 %

Appendix B. Documentation of the twenty-five cases of dental implants used for the reliability assessment

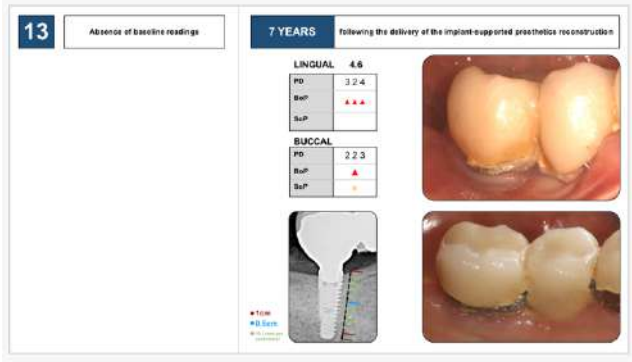



9
Presence of baseline readings
29 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 1.5
PD 3 3 3
PALATAL
PD 3 3 3
BUCCAL 1.5
PD 4 3 3
BoP
SoP
PALATAL
PD 3 3 3
BoP
SoP


10
Absence of baseline readings
11 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 2.5
PD 4 3 6
BoP
SoP
PALATAL
PD 6 4 5
BoP
SoP


11
Presence of baseline readings
5 YEARS
following the delivery of the implant-supported prosthetics reconstruction
LINGUAL 3.7
PD 3 3 3
BUCCAL
PD 3 2 3
LINGUAL 3.7
PD 5 4 3
BoP
SoP
BUCCAL
PD 4 2 3
BoP
SoP


12
Presence of baseline readings
6 YEARS
following the delivery of the implant-supported prosthetics reconstruction
LINGUAL 3.5
PD 3 1 3
BUCCAL
PD 3 2 3
LINGUAL 3.5
PD 3 1 3
BoP
SoP
BUCCAL
PD 3 1 3
BoP
SoP


13
Absence of baseline readings
7 YEARS
following the delivery of the implant-supported prosthetics reconstruction
LINGUAL 4.6
PD 3 2 4
BoP
SoP
BUCCAL
PD 2 2 3
BoP
SoP

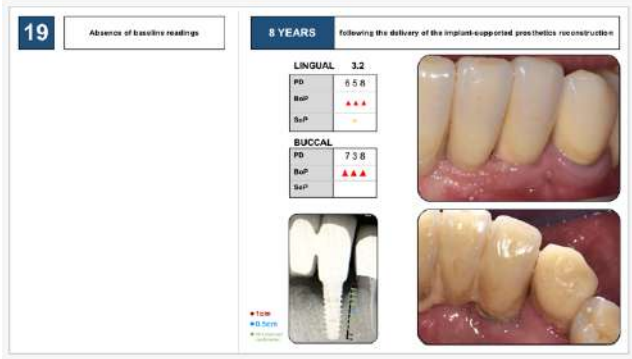

14
Presence of baseline readings
19 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 1.6
PD 3 2 3
PALATAL
PD 3 3 3
BUCCAL 1.6
PD 3 1 3
BoP
SoP
PALATAL
PD 5 6 7
BoP
SoP


15
Absence of baseline readings
12 YEARS
following the delivery of the implant-supported prosthetics reconstruction
LINGUAL 4.4
PD 5 3 4
BoP
SoP
BUCCAL
PD 5 4 6
BoP
SoP


16
Presence of baseline readings
20 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 1.6
PD 3 2 3
PALATAL
PD 4 2 4
BUCCAL 1.6
PD 3 2 3
BoP
SoP
PALATAL
PD 4 2 4
BoP
SoP


17
Absence of baseline readings
14 YEARS
following the delivery of the implant-supported prosthetics reconstruction
LINGUAL 3.7
PD 6 4 8
BoP ▲▲▲
SoP
BUCCAL
PD 6 5 8
BoP ▲▲▲
SoP
1cm
0.5cm


18
Presence of baseline readings
Absence of at the time of superstructure placement
BUCCAL 1.7
PD 3 2 3
PALATAL
PD 3 2 3
Absence at 1 year after delivery of the prosthetic restoration
9 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 1.7
PD 4 2 5
BoP ▲
SoP
PALATAL
PD 4 2 5
BoP ▲ ▲
SoP
1cm
0.5cm

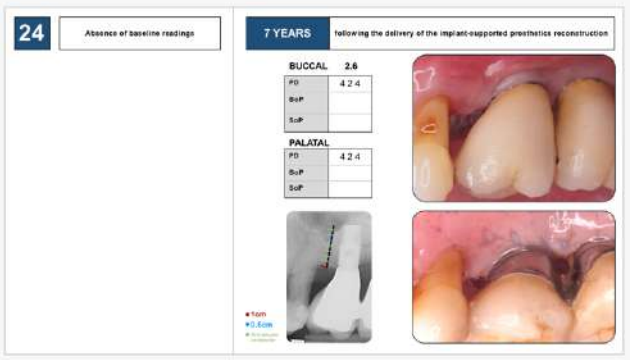

19
Absence of baseline readings
8 YEARS
following the delivery of the implant-supported prosthetics reconstruction
LINGUAL 3.2
PD 6 5 8
BoP ▲▲▲
SoP
BUCCAL
PD 7 3 8
BoP ▲▲▲
SoP
1cm
0.5cm

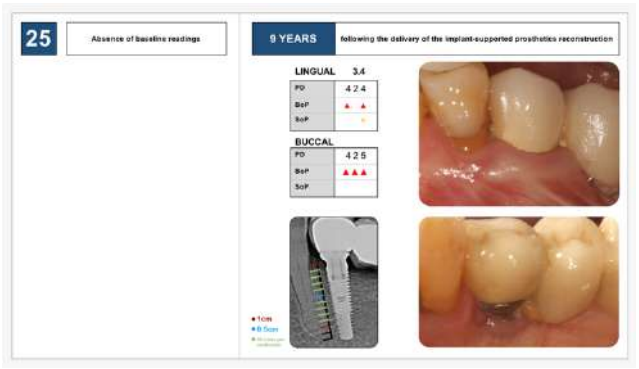

20
Presence of baseline readings
Absence of at the time of superstructure placement
BUCCAL 2.7
PD 3 2 3
PALATAL
PD 3 2 4
Absence at 1 year after delivery of the prosthetic restoration
10 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 2.7
PD 3 2 3
BoP
SoP
PALATAL
PD 4 2 4
BoP ▲ ▲
SoP
1cm
0.5cm


21
Absence of baseline readings
10 YEARS
following the delivery of the implant-supported prosthetics reconstruction
LINGUAL 3.6
PD 6 4 8
BoP ▲▲▲
SoP
BUCCAL
PD 6 5 8
BoP ▲▲▲
SoP
1cm
0.5cm


22
Absence of baseline readings
4 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 1.6
PD 8 6 6
BoP ▲▲▲
SoP
BUCCAL
PD 7 4 5
BoP ▲▲▲
SoP
1cm
0.5cm


23
Absence of baseline readings
3 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 1.6
PD 4 2 3
BoP ▲
SoP
BUCCAL
PD 4 2 4
BoP
SoP
1cm
0.5cm


24
Absence of baseline readings
7 YEARS
following the delivery of the implant-supported prosthetics reconstruction
BUCCAL 2.6
PD 4 2 4
BoP
SoP
PALATAL
PD 4 2 4
BoP
SoP
1cm
0.5cm


25
Absence of baseline readings
9 YEARS
following the delivery of the implant-supported prosthetics reconstruction
LINGUAL
3.4
PD
4 2 4
BoP
SoP
BUCCAL
PD
4 2 5
BoP
SoP