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CLINICAL ORAL IMPLANTS RESEARCH **WILEY**

Diagnosis of peri-implantitis in the absence of baseline data: A diagnostic accuracy study

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Abstract

Objectives: The aim of the present study was to evaluate the diagnostic accuracy of clinical and radiographic evaluations made at a single time point during follow-up in identifying (a) a history of peri-implant bone loss and (b) the presence of peri-implantitis.

Material & Methods: 427 patients provided with implant-supported reconstructions 9 years earlier were evaluated clinically by Probing Pocket Depth, Bleeding or Suppuration on Probing (PPD, BoP & SoP) and radiographically. Bone levels were assessed relative to the most coronal point of the intra-osseous part of the implant. A history of bone loss and diagnosis of peri-implantitis was confirmed through baseline documentation (direct evidence). Diagnostic accuracy of radiographic bone levels at 9 years and clinical findings (indirect evidence/secondary case definition) in identifying a history of bone loss and peri-implantitis were evaluated through correlation and multilevel regression analyses as well as receiver operating characteristic curves. Results were expressed as sensitivity/specificity and area under the curve (AUC).

Results: Bone levels observed at 9 years were highly accurate in identifying pronounced bone loss (>2 mm; AUC = 0.96; 95% CI 0.95–0.98). In the absence of baseline documentation, a secondary case definition based on the presence of BoP/SoP & bone level ≥ 1 mm (indirect evidence) provided the overall best diagnostic accuracy (AUC = 0.80; 95% CI 0.77–0.82) in identifying peri-implantitis cases (direct evidence: BoP/SoP & bone loss > 0.5 mm). Moderate/severe peri-implantitis (BoP/SoP & bone loss > 2 mm) was most accurately identified by the combination of BoP/SoP & bone level ≥ 2 mm (AUC = 0.93; 95% CI 0.91–0.96). Sensitivity of the secondary case definition suggested by the 2017 World Workshop of Periodontology (WWP) (BoP/SoP ≥ 1 site & bone level ≥ 3 mm & PPD ≥ 6 mm) was low.

Conclusions: The present results underline the importance of baseline documentation for the correct diagnosis of peri-implantitis, especially in its early/incipient forms. The secondary case definition of peri-implantitis suggested at the 2017 WWP demonstrated a high level of specificity but low sensitivity. Moderate/severe peri-implantitis was most accurately identified by the combination of BoP/SoP & bone level ≥ 2 mm.

1 | INTRODUCTION

Peri-implantitis is a plaque-associated pathological condition occurring in tissues around dental implants, characterized by inflammation in the peri-implant mucosa and subsequent progressive loss of supporting bone (Berglundh et al., 2018; Schwarz et al., 2018). Studies have shown that the prevalence of peri-implantitis ranges from 10% to 40% depending on case definitions (Derks, Schaller, Hakansson, et al., 2016; Rodrigo et al., 2018; Romandini et al., 2019, 2020b; Vignoletti et al., 2019; Wada et al., 2019) and that the progression of the disease follows a non-linear and accelerating pattern and may result in implant loss (Derks, Schaller, Håkansson, et al., 2016; Karlsson et al., 2019).

The diagnosis of peri-implantitis is based on the presence of bleeding (BoP) and/or suppuration (SoP) on gentle probing, increased probing pocket depth (PPD) and radiographic evidence of bone loss (Berglundh et al., 2018). According to this case definition presented at the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (2017 WWP), baseline/reference assessments of PPD and marginal bone levels constitute direct evidence for the diagnosis of peri-implantitis. In clinical reality, however, baseline readings may frequently not be available (e.g., implants placed in other settings). The lack of previous clinical and radiographic documentation may also be a limitation in epidemiological research, exemplified by the fact that only few studies were able to evaluate the prevalence and risk indicators of peri-implantitis using baseline data (e.g., Derks, Schaller, Hakansson, et al., 2016; Wada et al., 2019).

To facilitate the diagnostic process of peri-implantitis in the absence of baseline data, secondary case definitions based on indirect evidence of disease have been suggested. The VIII European Workshop on Periodontology (VIII EWP) proposed the findings of a vertical distance ≥2 mm from the expected marginal bone level in radiographs together with BoP/SoP to be consistent with a diagnosis of peri-implantitis (Sanz & Chapple, 2012). At the 2017 WWP, this secondary case definition for peri-implantitis (absence of baseline documentation) was revised. Thus, in addition to BoP/SoP, the findings of a PPD ≥6 mm together with a bone level of ≥3 mm apical to the most coronal portion of the intra-osseous part of the implant were suggested for the diagnosis (Berglundh et al., 2018).

In the absence of baseline data, threshold levels and the choice of parameters are critical for discriminating between cases of peri-implant mucositis and peri-implantitis. No studies, however, have validated the proposed secondary case definitions to be used in the absence of a baseline documentation. The aim of the present study was to evaluate the diagnostic accuracy of clinical and radiographic evaluations made at a single time point during follow-up (indirect evidence) in identifying (a) a history of bone loss and (b) the presence of peri-implantitis, as assessed by direct evidence.

2 | MATERIAL & METHODS

The present diagnostic accuracy study is reported according to the STARD 2015 Statement (STAndards for the Reporting of Diagnostic Accuracy Studies) (Bossuyt et al., 2015). It was conducted in accordance with the Helsinki Declaration of human studies, and the initial research protocol was approved by the regional Ethical Committee, Gothenburg, Sweden (Dnr 290–10) and registered at ClinicalTrials. gov (NCT01825772). All participants have provided their informed consent prior to the inclusion in the study.

2.1 | Study sample and baseline documentation

The patient sample was previously described (Derks et al., 2015; Derks, Håkansson, et al., 2015; Derks, Schaller, Hakansson, et al., 2016). Briefly, 4,716 subjects who received implant-supported restorative therapy in 2003 were randomly selected from the national data register of the Swedish Social Insurance Agency. Subsequently, informed consent was requested and dental records were obtained from the respective dental clinics. Nine years after the restorative therapy, a subsample of 900 randomly selected subjects was invited to a free-of-cost examination at a conveniently located dental clinic. A total of 596 subjects attended the 9-year examination.

Baseline radiographs were obtained from patient files. Images illustrating bone levels at 12 months after prosthetic loading were considered as ideal. If absent, images from 0 to 24 months were accepted as baseline. Readable radiographic documentation at baseline was available for 1,577 implants in 427 patients (Figure 1).

2.2 | 9-year examination

Examinations were carried out by previously calibrated specialists in periodontics. The following clinical parameters were recorded at the mesial, buccal, distal, and lingual aspects of each implant:

- PPD (mm): Measured with a manual periodontal probe (PCP15; Hu-Friedy);
- BoP (no/yes): Within 15 s following pocket probing;
- SoP (no/yes): Within 15 s following pocket probing.

New radiographs of implant sites were also obtained.

2.3 | Assessment of bone levels at baseline and 9 years

Marginal bone levels at baseline and at 9 years were measured (ImageJ 1.48a; Wayne Rasband, National Institutes of Health) using the most coronal point of the intra-osseous part of the implant as reference. The inter-thread pitch distance or the length of the implant was used for the calibration of the "apical-coronal" measurements in each radiograph. The largest value of the mesial and distal readings was recorded. Bone level assessments were performed by two examiners. Six months after the initial evaluation, radiographs of 50 patients were remeasured, revealing inter- and intra-examiner measurement errors of 0.40 ± 0.36 and 0.34 ± 0.37 mm, respectively.

2.4 | Case definitions: Bone loss and peri-implantitis (Direct evidence)

Bone loss was calculated as the difference between the marginal bone levels assessed at 9 years and at baseline (direct evidence; Figure A1). Different thresholds for bone loss were chosen (>0.5, >1 & >2 mm). Cases of peri-implantitis assessed by direct evidence were defined as the presence of BoP/SoP in combination with different thresholds of radiographic bone loss: >0.5, >1 & >2 mm. Bone loss > 2 mm together with BoP/SoP indicated moderate/severe peri-implantitis.

2.5 | Data analysis

Data analysis was performed using STATA version 13.1 software (StataCorp) and SPSS 24.0 software (IBM Corp). Continuous variables were described by means ($\pm$standard deviation) and categorical variables by frequency distributions (percentage).

2.5.1 | Identifying bone loss through indirect evidence (absence of baseline documentation)

Initially, the correlation between bone levels at 9 years and bone loss was evaluated through Spearman rho. We used a multilevel linear regression analysis (lower level: implant; higher level: patient) to estimate a correlation coefficient and to adjust for clustering and potential confounding. Variables considered included jaw, region, neighboring structure (tooth, implant, edentulous), and type of implant. Then, receiver operating characteristic (ROC) curves were obtained (Gasparini et al., 2015) and the area under the ROC curve (AUC) with 95% confidence intervals (95% CI) was evaluated according to the criteria described by Swets (1988).

Finally, different thresholds of bone levels (from 0.5 to 5 mm) at 9 years were tested for their diagnostic accuracy in identifying bone loss (>0.5, >1, >2 mm). Results were reported as sensitivity, specificity, predictive values, and AUC.

2.5.2 | Identifying peri-implantitis through indirect evidence (absence of baseline documentation)

The ability of PPD at 9 years to identify peri-implantitis was evaluated through ROC curves and associated AUC. The diagnostic accuracy of single clinical parameters and their different combinations at 9 years was also evaluated and described by sensitivity, specificity, predictive values, and AUC. Then, the most accurate thresholds (as identified through the highest AUC) for bone levels and
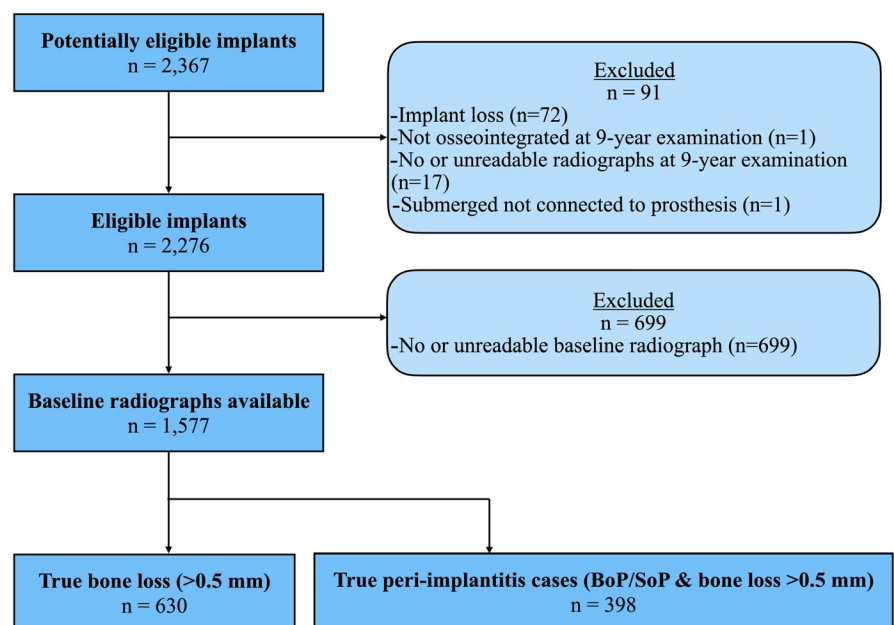

FIGURE 1 STARD 2015 flow diagram. From the 2,276 eligible implants (596 subjects), 699 implants (and 169 subjects) were excluded due to the lack of readable baseline radiographs resulting in a study population of 1,577 implants (427 subjects). n, number of implants

clinical parameters were combined to find ideal cutoffs in identifying peri-implantitis. Simultaneously, the diagnostic performance of secondary case definitions for peri-implantitis (absence of baseline documentation) suggested by the VIII EWP and the 2017 WWP was explored.

3 | RESULTS

Tables 1 and 2 provide descriptive data of the study population of participants and implants. The prevalence of peri-implantitis as assessed by direct evidence was 45.2% at patient-level and 25.2% at implant-level (case definition: presence of BoP/SoP & bone loss > 0.5 mm). Bone loss > 0.5 mm was detected in 65.1% of the patients and at 40.0% of the implants. Table 3 provides the clinical and radiographic characteristics of the implants affected by peri-implantitis. SoP was present at 19.9% of implants, and PPD ≥ 4 mm was noted at 71.3% of the peri-implantitis cases. PPD ≥ 6 mm was found at 34.4%, and a bone level ≥ 3 mm was present at 26.6% of affected implants.

TABLE 1 Characteristics of the study participants

Patients (n = 427)	
Age in 2003 (years), mean (SD)	62.5 (±9.4)
Sex, N (%)	
Female	239 (56.0%)
Male	188 (44.0%)
Smoking status (2003), N (%)	
Yes	49 (11.5%)
No	378 (88.5%)
Periodontitis status (9-y examination), N (%)	
Healthy	259 (60.7%)
Periodontitis	100 (23.4%)
Edentulous	68 (15.9%)
Surgical phase, N (%)	
General practitioner	96 (22.5%)
Specialist	331 (77.5%)
Prosthetic phase, N (%)	
General practitioner	316 (74.0%)
Specialist	111 (26.0%)
Peri-implant health[a], N (%)	
Healthy (Absence of BoP/SoP)	98 (23.0%)
Peri-implant mucositis (BoP/SoP & bone loss ≤ 0.5 mm)	136 (31.8%)
Peri-implantitis (BoP/SoP & bone loss > 0.5 mm)	193 (45.2%)
Presence of bone loss (>0.5 mm)[a], N (%)	
No	149 (34.9%)
Yes	278 (65.1%)

[a]The worst status was considered for subjects with >1 implants.

3.1 | Identifying bone loss through indirect evidence (absence of baseline documentation)

A statistically significant strong positive correlation between bone loss and bone level at 9 years was observed (r = 0.78; p < .001). Considering only implants evaluated through intraoral radiographs, a similar correlation was noted (r = 0.80; p < .001). Results of the multilevel linear regression analysis did not indicate any confounding effect of any of the background variables tested. The coefficient for bone level at 9 years in predicting bone loss was 0.69 (95% CI 0.66–0.71; p < .001) (Figure A2).

Single assessments of bone levels at 9 years were fairly accurate in identifying bone loss with a cutoff of >0.5 mm (AUC = 0.77; 95% CI 0.75–0.80) and >1 mm (AUC = 0.86; 95% CI 0.84–0.89) (Figure A3). Bone levels were highly accurate in detecting bone loss > 2 mm (AUC = 0.96; 95% CI 0.95–0.98) (Figure 2) and close to perfect in identifying bone loss > 3 mm and upward.

TABLE 2 Characteristics of the study implants

Implants (n = 1,577)	
Jaw, N (%)	
Maxilla	942 (59.7%)
Mandible	635 (40.3%)
Position, N (%)	
Anterior (canine-canine)	657 (41.7%)
Posterior	920 (58.3%)
Retention of supraconstruction, N (%)	
Screw-retained	1,250 (79.3%)
Cemented	286 (18.1%)
Missing data	41 (2.6%)
Design of supraconstruction, N (%)	
Single unit	185 (11.7%)
Multi unit	1,392 (88.3%)
Implant brand, N (%)	
Straumann	500 (31.7%)
Nobel	628 (39.8%)
Astra	274 (17.4%)
Other	175 (11.1%)
Type of radiograph, N (%)	
Intraoral	1,249 (79.2%)
Panoramic	328 (20.8%)
Peri-implant health, N (%)	
Healthy (Absence of BoP/SoP)	954 (60.50%)
Peri-implant mucositis (BoP/SoP & bone loss ≤ 0.5 mm)	556 (35.3%)
Peri-implantitis (BoP/SoP & bone loss > 0.5 mm)	398 (25.2%)
Presence of bone loss (>0.5 mm), N (%)	
No	947 (60.1%)
Yes	630 (39.9%)

Considering thresholds of bone levels, the highest accuracy to identify bone loss > 0.5 mm was observed for bone levels ≥ 1 mm (sensitivity = 68.3%; specificity = 73.5%; AUC = 0.71) and ≥1.5 mm

(sensitivity = 53.0%; specificity = 89.3%; AUC = 0.71) (Table 4). For the identification of bone loss > 1 mm, the highest accuracy was noted for bone level ≥ 1.5 mm (sensitivity = 74.9%; specificity = 84.6%;

TABLE 3 Clinical and radiographic characteristics of implants diagnosed with peri-implantitis according to different thresholds of bone loss

Implants with peri-implantitis			
	BoP/SoP + Bone loss > 0.5 mm (n = 398)	BoP/SoP + Bone loss > 1 mm (n = 235)	BoP/SoP + Bone loss > 2 mm (n = 128)
Clinical characteristics[a]			
BoP ≥ 1 site, n (%)	397 (99.8%)	234 (99.6%)	127 (99.2%)
BoP ≥ 3 sites, n (%)	182 (46.0%)	123 (52.3%)	84 (65.6%)
SoP ≥ 1 site, n (%)	79 (19.9%)	66 (28.1%)	52 (40.6%)
SoP ≥ 3 sites, n (%)	31 (7.8%)	28 (11.9%)	28 (21.9%)
Both BoP/SoP ≥ 1 site, n (%)	398 (100.0%)	235 (100.0%)	128 (100.0%)
Maximum PPD, mean ± SD	4.8 ± 1.9	5.2 ± 2.1	5.9 ± 2.3
PPD ≥ 2 mm, n (%)	392 (99.8%)	233 (99.6%)	127 (99.2%)
PPD ≥ 3 mm, n (%)	361 (91.9%)	217 (92.7%)	122 (95.3%)
PPD ≥ 4 mm, n (%)	280 (71.3%)	182 (77.8%)	110 (95.9%)
PPD ≥ 5 mm, n (%)	202 (51.4%)	142 (60.7%)	91 (71.1%)
PPD ≥ 6 mm, n (%)	135 (34.4%)	100 (42.7%)	75 (58.6%)
PPD ≥ 7 mm, n (%)	69 (17.6%)	59 (25.2%)	50 (39.1%)
Radiographic characteristics			
Bone loss, mean ± SD	1.9 ± 1.5	2.6 ± 1.6	3.6 ± 1.6
Bone level, mean ± SD	2.2 ± 1.9	3.0 ± 2.0	4.2 ± 1.9
Bone level ≥ 0.5 mm, n (%)	343 (86.2%)	221 (94.0%)	127 (99.2%)
Bone level ≥ 1 mm, n (%)	288 (72.4%)	202 (86.0%)	127 (99.2%)
Bone level ≥ 2 mm, n (%)	180 (45.2%)	159 (67.7%)	119 (93.0%)
Bone level ≥ 3 mm, n (%)	106 (26.6%)	100 (42.6%)	93 (72.7%)
Bone level ≥ 4 mm , n (%)	60 (15.1%)	59 (25.1%)	57 (44.5%)
Bone level ≥ 5 mm, n (%)	37 (9.3%)	36 (15.3%)	36 (28.1%)

[a]Total number of implants may vary due to missing data for BoP ≥ 3 sites (n = 5), SoP & SoP ≥ 3 sites (n = 3) and PPD (n = 55).
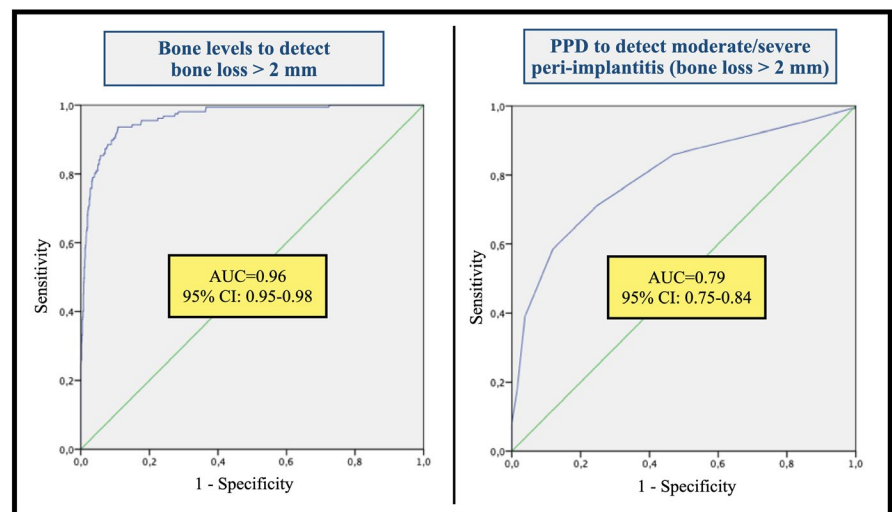

FIGURE 2 Receiver operating characteristic (ROC) curves for bone levels and PPD at 9 years in detecting bone loss > 2 and moderate/severe peri-implantitis (bone loss > 2 mm), respectively. AUC, area under the curve; PPD, probing pocket depth

TABLE 4 Diagnostic accuracy of different thresholds of bone levels for the detection of bone loss > 0.5 and >2 mm

Bone loss > 0.5 mm

	Bone level ≥ 0.5 mm	Bone level ≥ 1 mm	Bone level ≥ 1.5 mm	Bone level ≥ 2 mm	Bone level ≥ 2.5 mm	Bone level ≥ 3 mm	Bone level ≥ 3.5 mm	Bone level ≥ 4 mm	Bone level ≥ 4.5 mm	Bone level ≥ 5 mm
Prevalence% (95% CI)										39.9 (37.5–42.4)
Sensitivity% (95% CI)	83.8 (80.7–86.6)	68.3 (64.5–71.9)	53.0 (49.0–57.0)	39.8 (36.0–43.8)	28.1 (24.6–31.8)	21.1 (18.0–24.5)	16.2 (13.4–19.3)	11.3 (8.9–14.0)	7.9 (5.9–10.3)	6.8 (5.0–9.1)
Specificity% (95% CI)	45.8 (42.6–49.1)	73.5 (70.6–76.3)	89.3 (87.2–91.2)	94.8 (93.2–96.1)	97.9 (96.8–98.7)	98.7 (97.8–99.3)	99.2 (98.3–99.6)	99.5 (98.8–99.8)	99.9 (99.4–100.0)	100.0 (99.6–100.0)
AUC (95% CI)	0.65 (0.63–0.67)	0.71 (0.69–0.73)	0.71 (0.69–0.73)	0.67 (0.65–0.69)	0.63 (0.61–0.65)	0.60 (0.58–0.62)	0.58 (0.56–0.59)	0.55 (0.54–0.57)	0.54 (0.53–0.55)	0.53 (0.52–0.54)
PPV% (95% CI)	50.7 (47.6–53.8)	63.1 (59.4–66.8)	76.8 (72.5–80.7)	83.7 (79.0–87.7)	89.8 (84.8–93.7)	91.7 (86.0–95.7)	92.7 (86.2–96.8)	93.4 (85.3–97.8)	98.0 (89.6–100.0)	100.0 (91.8–100.0)
NPV% (95% CI)	81.0 (77.4–84.2)	77.7 (74.8–80.4)	74.1 (71.4–76.6)	70.3 (67.7–72.8)	67.2 (64.6–69.6)	65.3 (62.8–67.8)	64.0 (61.5–66.5)	62.8 (60.3–65.2)	62.0 (59.5–64.4)	61.7 (59.2–64.2)

Bone loss > 2 mm

	Bone level ≥ 0.5 mm	Bone level ≥ 1 mm	Bone level ≥ 1.5 mm	Bone level ≥ 2 mm	Bone level ≥ 2.5 mm	Bone level ≥ 3mm	Bone level ≥ 3.5 mm	Bone level ≥ 4 mm	Bone level ≥ 4.5 mm	Bone level ≥ 5 mm
Prevalence% (95% CI)										10.0 (8.5–11.5)
Sensitivity% (95% CI)	99.4 (96.5–100.0)	99.4 (96.5–100.0)	95.5 (91.0–98.2)	93.0 (87.8–96.5)	80.9 (73.9–86.7)	70.7 (62.9–77.7)	58.6 (50.5–66.4)	41.4 (33.6–49.5)	30.6 (23.5–38.4)	26.1 (19.4–33.7)
Specificity% (95% CI)	37.7 (35.1–40.3)	63.0 (60.5–65.5)	79.9 (77.8–82.0)	89.2 (87.4–90.7)	95.1 (93.8–96.1)	97.6 (96.7–98.3)	98.7 (98.0–99.2)	99.2 (98.6–99.6)	99.8 (99.4–100.0)	99.9 (99.5–100.0)
AUC (95% CI)	0.69 (0.67–0.70)	0.81 (0.80–0.83)	0.88 (0.86–0.90)	0.91 (0.89–0.93)	0.88 (0.85–0.91)	0.84 (0.81–0.88)	0.79 (0.75–0.83)	0.70 (0.66–0.74)	0.65 (0.62–0.69)	0.63 (0.60–0.66)
PPV% (95% CI)	15.0 (12.9–17.3)	22.9 (19.8–26.3)	34.5 (30.0–39.2)	48.7 (42.9–54.5)	64.5 (57.4–71.1)	76.6 (68.8–83.2)	83.6 (75.4–90.0)	85.5 (75.6–92.5)	94.1 (83.8–98.8)	95.3 (84.2–99.4)
NPV% (95% CI)	99.8 (99.0–100.0)	99.9 (99.4–100.0)	99.4 (98.7–99.8)	99.1 (98.5–99.6)	97.8 (96.9–98.5)	96.8 (95.7–97.6)	95.6 (94.4–96.6)	93.9 (92.5–95.0)	92.9 (91.4–94.1)	92.4 (91.0–93.7)

Abbreviations: AUC, Area under the curve; PPV, Positive predictive value; NPV, Negative predictive value

AUC = 0.80) (Table A1). Bone loss > 2 mm was best identified by bone level ≥ 2 mm (sensitivity = 93.0%; specificity = 89.2%; AUC = 0.91) (Table 4).

3.2 | Identifying peri-implantitis through indirect evidence (absence of baseline documentation)

Assessment of PPD at 9 years demonstrated low accuracy in identifying peri-implantitis with a threshold for bone loss > 0.5 mm (AUC = 0.69; 95% CI 0.66–0.73) (Figure 2 and Figure A4). No clinical parameter, either alone or in combination, increased the diagnostic accuracy of BoP/SoP ≥ 1 sites in identifying peri-implantitis cases with bone loss > 0.5 mm (sensitivity = 100.0%; specificity = 52.8%; AUC = 0.76) (Table 5). Second to BoP/SoP, the highest sensitivity was observed for PPD ≥ 4 mm, either alone or in combination with BoP/SoP (sensitivity = 71.2%; specificity = 57.0%–71.0%; AUC = 0.64–0.71). The highest specificity was observed for SoP ≥ 3 sites (sensitivity = 7.8%; specificity = 99.2%; AUC = 0.54).

The most accurate combination of parameters was BoP/SoP ≥ 1 sites together with bone levels ≥ 1 mm, which demonstrated a sensitivity of 72.4%, a specificity of 86.8%, and an AUC = 0.80. The secondary case definition in the absence of baseline documentation suggested by the 2017 WWP (BoP/SoP, PPD ≥ 6 mm & bone level ≥ 3 mm) had a sensitivity of 15.4%, a specificity of 99.5%, and an AUC = 0.57 in identifying peri-implantitis cases (BoP/SoP & bone loss > 0.5 mm) (Table 6). The VIII EWP case definition (BoP/SoP & bone level ≥ 2 mm) had a corresponding sensitivity of 45.2%, a specificity of 97.4%, and an AUC = 0.71.

The diagnostic accuracy for the identification of peri-implantitis with bone loss > 1 mm is illustrated in the appendix (Tables A1-3). For moderate/severe peri-implantitis (BoP/SoP & bone loss > 2 mm), PPD at 9 years showed fair diagnostic accuracy (AUC = 0.79; 95% CI 0.75–0.84) (Figure A4). Different combinations of clinical parameters slightly increased the diagnostic accuracy of BoP/SoP ≥ 1 sites alone (sensitivity = 100.0%; specificity = 43.0%; AUC = 0.71), with the highest accuracy noted for either PPD ≥ 4 mm or PPD ≥ 5 mm together with BoP/SoP (sensitivity = 71.1%–85.9%; specificity = 64.3%–79.6%; AUC = 0.75) (Table 5). Second to BoP/SoP, the highest sensitivity was observed for PPD ≥ 4 mm either alone or in combination with BoP/SoP (sensitivity = 85.9%; specificity = 53.0%–64.3%; AUC = 0.69–0.75). The highest specificity was noted for SoP ≥ 3 sites (sensitivity = 21.9%; specificity = 99.2%; AUC = 0.61). Cases of moderate/severe peri-implantitis were detected by the 2017 WWP secondary case definition (BoP/SoP, PPD ≥ 6 mm & bone level ≥ 3 mm) with a sensitivity of 43.8%, a specificity of 99.3% and an AUC of 0.72 (Table 6). The corresponding values for the VIII EWP secondary case definition (BoP/SoP & bone level ≥ 2 mm) were 93.0%, 93.7%, and 0.93, which was thereby identified as the combination with the highest diagnostic accuracy in identifying moderate/severe peri-implantitis through indirect evidence.

4 | DISCUSSION

The present study evaluated the diagnostic accuracy of clinical and radiographic findings from a single time point during follow-up in identifying bone loss and peri-implantitis. Results indicated that bone loss using >0.5 and >1.0 mm as thresholds was only partially identified by bone levels observed at 9 years. Bone levels, however, were highly accurate in identifying more pronounced bone loss (>2 mm). In the absence of baseline documentation, the secondary case definition based on the presence of BoP/SoP & bone level ≥ 1 mm provided the overall best diagnostic accuracy in identifying peri-implantitis cases (BoP/SoP & bone loss > 0.5 mm). Moderate/severe peri-implantitis (BoP/SoP & bone loss > 2 mm) was most accurately identified by the combination of BoP/SoP & bone level ≥ 2 mm. Adding PPD, SoP, and/or extent of BoP to secondary case definitions of peri-implantitis reduced the diagnostic accuracy, explained by the low sensitivity of these parameters. Sensitivity of the secondary case definition suggested by the 2017 WWP was also low.

The 2017 WWP highlighted the importance of baseline documentation for correct diagnosis of peri-implantitis but also suggested a secondary case definition to be used in the absence of baseline data. The low sensitivity observed for this secondary case definition in the present study implies that cases of incipient/early peri-implantitis are frequently left undiagnosed. Clinicians should be aware of the limited diagnostic value of this secondary case definition, given the importance of early diagnosis of peri-implantitis. Cases with incipient peri-implantitis are the ones amenable of less invasive (i.e., non-surgical) treatment (Figuero et al., 2014) and demonstrate most favorable long-term outcomes following therapy (Ravidà, Saleh, et al., 2020; Ravidà, Siqueira, et al., 2020).

The low sensitivity of the 2017 WWP secondary case definition is explained not only by its high threshold in terms of bone level, but also by adding PPD as a parameter. In the present cohort, 66% of implants with peri-implantitis presented with PPD < 6 mm and almost one third with PPD ≤3 mm. Deep PPD has previously been shown to be related to the presence of peri-implantitis (Monje, Caballé-Serrano, et al., 2018; Monje, Insua, et al., 2018; Ramanauskaite et al., 2018; Rodrigo et al., 2018; Vignoletti et al., 2019), but studies have also indicated that peri-implantitis may also manifest with shallow PPD (Fransson et al., 2008; Romandini et al., 2020a). Mucosal recession may be one explanation as to why peri-implantitis was not necessarily related to an increase in PPD (Monje, Insua, et al., 2018; Romandini et al., 2020a). Another possible reason for the limited value of PPD in the identification of peri-implantitis in the present cohort is that probing was performed without removing implant restorations, which has previously been shown to results in a reduced correlation between PPD and marginal bone levels (Serino et al., 2013).

Despite the low sensitivity of PPD and the presence of SoP, deep probing (PPD ≥ 7 mm) but also SoP demonstrated a very high specificity (>96%) in identifying peri-implantitis cases. The high specificity of SoP was also observed by Ramanauskaite et al. (2018), who only

TABLE 5 Diagnostic accuracy of different clinical parameters for the detection of peri-implantitis with bone loss > 0.5 and >2 mm

Peri-implantitis (BoP/SoP+ & Bone loss > 0.5 mm)

Prevalence% (95% CI): 25.2 (23.1–27.5)

	BoP+ ≥1 site	BoP+ ≥3 sites	SoP+ ≥1 site	SoP+ ≥3 sites	BoP + or SoP+ ≥1 site	PPD ≥ 4 mm	PPD ≥ 5 mm	PPD ≥ 6 mm	PPD ≥ 7 mm	PPD≥4 mm & BoP+ ≥ site	PPD≥5 mm & BoP+ ≥ site	PPD≥6 mm & BoP+ ≥ site	PPD≥7 mm & BoP+ ≥ site
Sensitivity% (95% CI)	99.7 (98.6–100.0)	46.0 (41.0–51.0)	19.8 (16.0–24.1)	7.8 (5.4–10.9)	100.0 (99.1–100.0)	71.2 (66.5–75.7)	51.4 (46.3–56.4)	34.4 (29.7–39.3)	17.7 (13.9–21.7)	71.2 (66.5–75.7)	51.4 (46.3–56.4)	34.4 (29.7–39.3)	17.6 (13.9–21.7)
Specificity% (95% CI)	53.1 (50.2–56.0)	84.6 (82.4–86.6)	96.1 (94.8–97.1)	99.2 (98.6–99.6)	52.8 (49.9–55.7)	57.0 (54.1–60.0)	79.3 (76.8–81.6)	90.5 (88.7–92.2)	97.0 (95.8–97.9)	71.0 (68.3–73.7)	84.6 (82.3–86.6)	92.2 (90.5–93.7)	97.2 (96.0–98.1)
AUC (95% CI)	0.76 (0.75–0.78)	0.65 (0.63–0.68)	0.58 (0.56–0.60)	0.54 (0.52–0.55)	0.76 (0.75–0.78)	0.64 (0.61–0.67)	0.65 (0.63–0.68)	0.62 (0.60–0.65)	0.57 (0.55–0.59)	0.71 (0.69–0.74)	0.68 (0.65–0.71)	0.63 (0.61–0.66)	0.57 (0.55–0.59)
PPV% (95% CI)	41.8 (38.6–45.0)	50.1 (44.9–55.4)	63.2 (54.1–71.6)	77.5 (61.5–89.2)	41.7 (38.6–44.9)	36.6 (33.2–40.1)	46.3 (41.6–51.1)	55.8 (49.3–62.1)	67.0 (57.0–75.9)	46.1 (42.1–50.2)	53.7 (48.5–58.8)	60.5 (53.8–67.0)	68.3 (58.3–77.2)
NPV% (95% CI)	99.8 (99.1–100.0)	82.3 (80.0–84.4)	78.0 (75.8–80.1)	76.1 (73.9–78.2)	100.0 (99.4–100.0)	85.1 (82.3–87.5)	82.4 (80.0–84.6)	79.8 (77.5–82.0)	77.2 (74.9–79.3)	87.7 (85.3–89.7)	83.3 (81.0–85.4)	80.1 (77.9–82.3)	77.2 (74.9–79.4)

	PPD ≥ 4 mm & BoP+ ≥3 sites	PPD ≥ 5 mm & BoP+ ≥3 sites	PPD ≥ 6 mm & BoP+ ≥3 sites	PPD ≥ 7 mm & BoP+ ≥3 sites	PPD ≥ 4 mm & SoP+ ≥1 site	PPD ≥ 5 mm & SoP+ ≥1 site	PPD ≥ 6 mm & SoP+ ≥1 site	PPD ≥ 7 mm & SoP+ ≥1 site	PPD≥4 mm & BoP + or SoP+ ≧ 1	PPD≥5 mm & BoP + or SoP+ ≧ 1	PPD≥6 mm & BoP + or SoP+ ≧ 1	PPD≥7 mm & BoP + or SoP+ ≧ 1
Sensitivity% (95% CI)	40.2 (35.3–45.2)	34.1 (29.4–39.0)	26.0 (21.7–30.6)	14.8 (11.4–18.7)	19.3 (15.6–23.6)	14.2 (10.9–18.1)	9.9 (7.2–13.3)	18.1 (14.4–22.2)	71.2 (66.5–75.7)	51.4 (46.3–56.4)	34.4 (29.7–39.3)	17.6 (13.9–21.7)
Specificity% (95% CI)	88.9 (87.0–90.7)	92.6 (91.0–94.1)	95.9 (94.6–97.0)	98.2 (97.3–98.9)	96.1 (94.8–97.2)	97.4 (96.3–98.3)	98.9 (98.2–99.4)	96.5 (95.2–97.5)	70.9 (68.2–73.6)	84.6 (82.3–86.6)	92.2 (90.5–93.7)	97.2 (96.0–98.1)
AUC (95% CI)	0.65 (0.62–0.67)	0.63 (0.61–0.66)	0.61 (0.59–0.63)	0.56 (0.55–0.58)	0.58 (0.56–0.60)	0.56 (0.54–0.58)	0.54 (0.53–0.56)	0.57 (0.55–0.59)	0.71 (0.68–0.74)	0.68 (0.65–0.71)	0.63 (0.61–0.66)	0.57 (0.55–0.59)
PPV% (95% CI)	55.8 (49.8–61.7)	61.8 (54.9–68.2)	68.9 (60.8–76.3)	74.4 (63.2–83.6)	63.3 (54.1–71.9)	65.9 (54.8–75.8)	76.5 (62.5–87.2)	64.0 (54.3–72.9)	46.1 (42.0–50.1)	53.7 (48.5–58.8)	60.5 (53.8–67.0)	68.3 (58.3–77.2)
NPV% (95% CI)	81.0 (78.7–83.2)	80.2 (77.9–82.3)	78.8 (76.6–81.0)	76.8 (74.5–79.0)	77.4 (75.1–79.6)	76.5 (74.3–78.7)	75.9 (73.7–78.1)	77.2 (74.9–79.3)	87.6 (85.3–89.7)	83.3 (81.0–85.4)	80.1 (77.9–82.3)	77.2 (74.9–79.4)

Peri-implantitis (BoP/SoP+ & Bone loss > 2 mm)

Prevalence% (95% CI): 8.1 (6.8–9.6)

	BoP+ ≥1 site	BoP+ ≥3 sites	SoP+ ≥1 site	SoP+ ≥3 sites	BoP + or SoP+ ≥1 site	PPD ≥ 4 mm	PPD ≥ 5 mm	PPD ≥ 6 mm	PPD ≥ 7 mm	PPD≥4 mm & BoP+ ≥ site	PPD≥5 mm & BoP+ ≥ site	PPD≥6 mm & BoP+ ≥ site	PPD≥7 mm & BoP+ ≥ site
Sensitivity% (95% CI)	99.2 (95.7–100.0)	65.6 (56.7–73.8)	40.6 (32.0–49.7)	21.9 (15.1–30.0)	100.0 (97.2–100.0)	85.9 (78.7–91.4)	71.1 (62.4–78.8)	58.6 (49.6–67.2)	39.1 (30.6–48.1)	85.9 (78.7–91.4)	71.1 (62.4–78.8)	58.6 (49.6–67.2)	39.1 (30.6–48.1)
Specificity% (95% CI)	43.2 (40.6–45.8)	80.7 (78.5–82.7)	95.0 (93.7–96.0)	99.2 (98.6–99.6)	43.0 (40.4–45.6)	53.0 (50.4–55.7)	75.3 (72.9–77.5)	88.0 (86.2–89.7)	96.2 (95.1–97.1)	64.3 (61.8–66.9)	79.6 (77.3–81.6)	89.4 (87.6–91.0)	96.3 (95.2–97.3)

(Continues)

TABLE 5 (Continued)

	BoP+ ≥1 site	BoP+ ≥3 sites	SoP+ ≥1 site	SoP+ ≥3 sites	BoP + or SoP+ ≥1 site	PPD ≥ 4 mm	PPD ≥ 5 mm	PPD ≥ 6 mm	PPD ≥ 7 mm	PPD≥4 mm & BoP+ ≥ site	PPD≥5 mm & BoP+ ≥ site	PPD≥6 mm & BoP+ ≥ site	PPD≥7 mm & BoP+ ≥ site
AUC (95% CI)	0.71 (0.70–0.73)	0.73 (0.69–0.77)	0.68 (0.63–0.72)	0.61 (0.57–0.64)	0.71 (0.70–0.73)	0.69 (0.66–0.73)	0.73 (0.69–0.77)	0.73 (0.69–0.78)	0.68 (0.63–0.72)	0.75 (0.72–0.78)	0.75 (0.71–0.79)	0.74 (0.70–0.78)	0.68 (0.63–0.72)
PPV% (95% CI)	13.4 (11.3–15.7)	23.1 (18.9–27.8)	41.6 (32.9–50.8)	70.0 (53.5–83.4)	13.4 (11.3–15.7)	14.4 (12.0–17.1)	20.9 (17.2–25.0)	31.0 (25.2–37.2)	48.5 (38.6–58.6)	18.1 (15.1–21.4)	24.2 (20.0–28.9)	33.6 (27.5–40.2)	49.5 (39.4–59.6)
NPV% (95% CI)	99.8 (99.1–100.0)	96.4 (95.1–97.3)	94.8 (93.5–95.8)	93.5 (92.1–94.7)	100.0 (99.4–100.0)	97.6 (96.3–98.6)	96.6 (95.3–97.6)	95.9 (94.6–96.9)	94.5 (93.2–95.6)	98.0 (96.9–98.9)	96.8 (95.6–97.7)	95.9 (94.7–96.9)	94.5 (93.2–95.6)

	PPD ≥ 4 mm & BoP+ ≥3 sites	PPD ≥ 5 mm & BoP+ ≥3 sites	PPD ≥ 6 mm & BoP+ ≥3 sites	PPD ≥ 7 mm & BoP+ ≥3 sites	PPD ≥ 4 mm & SoP+ ≥1 site	PPD ≥ 5 mm & SoP+ ≥1 site	PPD ≥ 6 mm & SoP+ ≥1 site	PPD ≥ 7 mm & SoP+ ≥1 site	PPD≥4 mm & BoP + or SoP+ ≥ 1	PPD≥5 mm & BoP + or SoP+ ≥ 1	PPD≥6 mm & BoP + or SoP+ ≥ 1	PPD≥7 mm & BoP + or SoP+ ≥ 1
Sensitivity% (95% CI)	60.9 (51.9–69.4)	57.8 (48.8–66.5)	50.8 (41.8–59.7)	34.4 (26.2–43.3)	39.1 (30.6–48.1)	37.5 (29.1–46.5)	31.2 (23.4–40.0)	24.2 (17.1–32.6)	85.9 (78.7–91.4)	71.1 (62.4–78.8)	58.6 (49.6–67.2)	39.1 (30.6–48.1)
Specificity% (95% CI)	85.3 (83.3–87.1)	89.7 (88.0–91.3)	94.0 (92.7–95.2)	97.6 (96.6–98.3)	95.0 (93.7–96.1)	95.1 (94.3–96.5)	96.8 (95.7–97.6)	98.6 (97.8–99.1)	64.3 (61.7–66.8)	79.6 (77.3–81.6)	89.4 (87.6–91.0)	96.3 (95.2–97.3)
AUC (95% CI)	0.73 (0.69–0.77)	0.74 (0.69–0.78)	0.72 (0.68–0.77)	0.66 (0.62–0.70)	0.67 (0.63–0.71)	0.66 (0.62–0.71)	0.64 (0.60–0.68)	0.61 (0.58–0.65)	0.75 (0.72–0.78)	0.75 (0.71–0.79)	0.74 (0.70–0.78)	0.68 (0.63–0.72)
PPV% (95% CI)	27.6 (22.4–33.2)	34.1 (27.8–40.8)	43.9 (35.8–52.3)	56.4 (44.7–67.6)	43.2 (33.9–53.0)	47.1 (36.1–58.2)	60.8 (46.1–74.2)	41.7 (32.7–51.0)	18.1 (15.1–21.4)	24.2 (20.0–28.9)	33.6 (27.5–40.2)	49.5 (39.4–59.6)
NPV% (95% CI)	96.0 (94.7–97.0)	95.9 (94.6–96.9)	95.4 (94.2–96.5)	94.2 (92.8–95.3)	94.4 (93.1–95.6)	94.3 (93.0–95.5)	93.9 (92.5–95.1)	93.4 (92.0–94.6)	98.0 (96.9–98.8)	96.8 (95.6–97.7)	95.9 (94.7–96.9)	94.5 (93.2–95.6)

Abbreviations: AUC, Area under the curve; PPV, Positive predictive value; NPV, Negative predictive value

TABLE 6 Diagnostic accuracy of different case definitions for the detection of peri-implantitis with bone loss > 0.5 and >2 mm in absence of baseline data

Peri-implantitis (BoP/SoP+ & Bone loss > 0.5 mm) — Prevalence% (95% CI): 25.2 (23.1–27.5)

Case definition	Sensitivity% (95% CI)	Specificity% (95% CI)	AUC (95% CI)	PPV% (95% CI)	NPV% (95% CI)
Bone level ≥ 3 mm & BoP/SoP ≥ 1 site & PPD ≥ 6 mm (2017 WWP)	15.4 (12.0–19.3)	99.6 (99.0–99.9)	0.57 (0.56–0.59)	92.4 (83.2–97.5)	77.7 (75.6–79.8)
Bone level ≥ 2 mm & BoP/SoP ≥ 1 site (VIII EWP)	45.2 (40.3–50.3)	97.4 (96.3–98.2)	0.71 (0.69–0.74)	85.3 (79.8–89.8)	84.0 (82.0–85.9)
Bone level ≥ 1 mm & BoP/SoP ≥ 1 site	72.4 (67.7–76.7)	86.8 (84.7–88.7)	0.80 (0.77–0.82)	64.9 (60.2–69.3)	90.3 (88.4–92.0)
Bone level ≥ 1 mm & BoP/SoP ≥ 1 site & PPD ≥ 4 mm	54.3 (49.2–59.2)	91.0 (89.2–92.6)	0.73 (0.70–0.75)	67.1 (61.7–72.2)	85.5 (83.4–87.4)
Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site	59.3 (54.3–64.2)	94.7 (93.3–95.9)	0.77 (0.75–0.80)	79.2 (74.1–83.7)	87.3 (85.4–89.1)
Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 4 mm	46.7 (41.7–51.8)	96.2 (94.9–97.2)	0.71 (0.69–0.74)	80.4 (74.7–85.4)	84.3 (82.3–86.2)

Peri-implantitis (BoP/SoP + & Bone loss > 2 mm) — Prevalence% (95% CI): 8.1 (6.8–9.6)

Case definition	Sensitivity% (95% CI)	Specificity% (95% CI)	AUC (95% CI)	PPV% (95% CI)	NPV% (95% CI)
Bone level ≥ 3 mm & BoP/SoP ≥ 1 site & PPD ≥ 6 mm (2017 WWP)	43.8 (35.0–52.8)	99.3 (98.7–99.7)	0.72 (0.67–0.76)	84.8 (73.9–92.5)	95.2 (94.0–96.3)
Bone level ≥ 2 mm & BoP/SoP ≥ 1 site (VIII EWP)	93.0 (87.1–96.7)	93.7 (92.3–94.9)	0.93 (0.91–0.96)	56.4 (49.4–63.2)	99.3 (98.8–99.7)
Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site	94.5 (89.1–97.8)	87.8 (86.0–89.4)	0.91 (0.89–0.93)	40.6 (35.0–46.4)	99.5 (98.9–99.8)
Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 4 mm	82.0 (74.3–88.3)	91.4 (89.8–92.8)	0.87 (0.83–0.90)	45.7 (39.1–52.3)	98.3 (97.4–98.9)
Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 5 mm	68.8 (60.0–76.6)	94.1 (92.7–95.2)	0.81 (0.77–0.85)	50.6 (42.9–58.2)	97.1 (96.1–98.0)
Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 6 mm	56.2 (47.2–65.0)	96.8 (95.8–97.7)	0.77 (0.72–0.81)	61.0 (51.6–69.9)	96.2 (95.0–97.1)
Bone level ≥ 2 mm & BoP/SoP ≥ 1 site & PPD ≥ 4 mm	81.2 (73.4–87.6)	95.4 (94.2–96.5)	0.88 (0.85–0.92)	61.2 (53.4–68.5)	98.3 (97.5–98.9)
Bone level ≥ 2 mm & BoP/SoP ≥ 1 site & PPD ≥ 5 mm	55.5 (46.4–64.3)	97.9 (97.1–98.6)	0.77 (0.72–0.81)	70.3 (60.4–79.0)	96.1 (95.0–97.1)
Bone level ≥ 2.5 mm & BoP/SoP ≥ 1 site	84.4 (76.9–90.2)	97.0 (96.0–97.8)	0.91 (0.88–0.94)	71.5 (63.6–78.6)	98.6 (97.8–99.1)
Bone level ≥ 2.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 4 mm	75.0 (66.6–82.2)	97.9 (97.1–98.6)	0.86 (0.83–0.90)	76.2 (67.8–83.3)	97.8 (96.9–98.5)
Bone level ≥ 2.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 5 mm	62.5 (53.5–70.9)	98.3 (97.5–98.9)	0.80 (0.76–0.85)	76.2 (66.9–84.0)	96.7 (95.7–97.6)
Bone level ≥ 2.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 6 mm	50.0 (41.0–59.0)	98.8 (98.1–99.3)	0.74 (0.70–0.79)	79.0 (68.5–87.3)	95.7 (94.6–96.7)

Abbreviations: AUC, Area under the curve. PPV, Positive predictive value. NPV, Negative predictive value.

noted SoP at implants affected by peri-implantitis. Consequently, while the absence of deep PPD and of SoP is of limited diagnostic value, clinicians may consider their presence as strong indicators of peri-implantitis.

Whenever baseline documentation is not available, a case definition based on BoP and/or SoP together with bone levels > 1 mm provided the best diagnostic accuracy in identifying peri-implantitis cases. However, this case definition still resulted in a significant number of false negative (27.6%) and false positive (13.2%) cases, which highlights the importance of baseline documentation, particularly for early/incipient cases of peri-implantitis. However, from the threshold of ≥ 2 mm and upwards, radiographic bone levels were highly accurate in identifying a history of previous bone loss. As a consequence, if the aim is to identify moderate/severe cases of peri-implantitis (bone loss > 2 mm), the secondary case definition suggested by the VIII EWP was highly accurate. As a consequence, surveillance studies targeting advanced cases of peri-implantitis and evaluating associated risk profiles may consider secondary case definitions to be sufficient, considering also the difficulties in retrieving baseline data (e.g., Rodrigo et al., 2018).

Interestingly, while bone loss was noted at 40.0% of implants, the prevalence of peri-implantitis was lower (25.2%), as 14.8% of the implants presented bone loss but no BoP/SoP. Similar results were also reported in other studies (e.g., Rodrigo et al., 2018). In the present study, soft tissue inflammation was assessed at a single time point, only. It is feasible that the health status of peri-implant soft tissues is not constant over long time periods. It is also possible that preventive and therapeutic measures provided to the patients during follow-up may have confounded the relationship between clinical and radiographic measures at the final examination.

The results of this investigation are relevant, as they represent an analysis of the diagnostic accuracy of currently recommended secondary cases definitions of peri-implantitis. The presence of baseline radiographs in the present cohort allowed the identification of peri-implantitis cases through direct evidence. The random sampling of study participants minimized the risk of selection bias and the fact that multiple clinicians performed the clinical examinations further strengthened the external validity of the present findings.

The main limitation of the present study is represented by the lack of baseline readings of PPD, which is part of the currently recommended case definition (direct evidence) of peri-implantitis (Berglundh et al., 2018). However, the value of PPD for the identification of peri-implantitis is questioned by the findings of the present analysis. The value of clinical parameters (PPD & BoP) in screening for bone loss, that is justification of radiographic evaluation, is reported elsewhere (Berglundh et al., 2020).

5 | CONCLUSIONS

The present results underline the importance of baseline documentation for the correct diagnosis of peri-implantitis, especially in its early/incipient forms. The secondary case definition of peri-implantitis suggested at the 2017 WWP demonstrated a high level of specificity but low sensitivity. Moderate/severe peri-implantitis was most accurately identified by the combination of BoP/SoP & bone level ≥ 2 mm.

CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

M. Romandini, J. Berglundh, J. Derks, M. Sanz and T. Berglundh contributed to conception, design and data analysis, drafted the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work.

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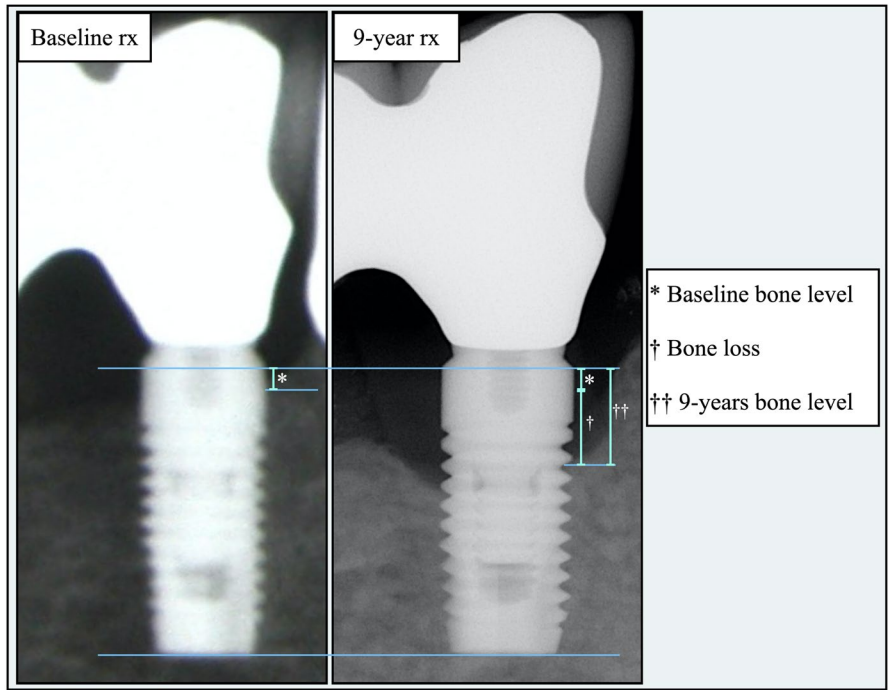
APPENDIX

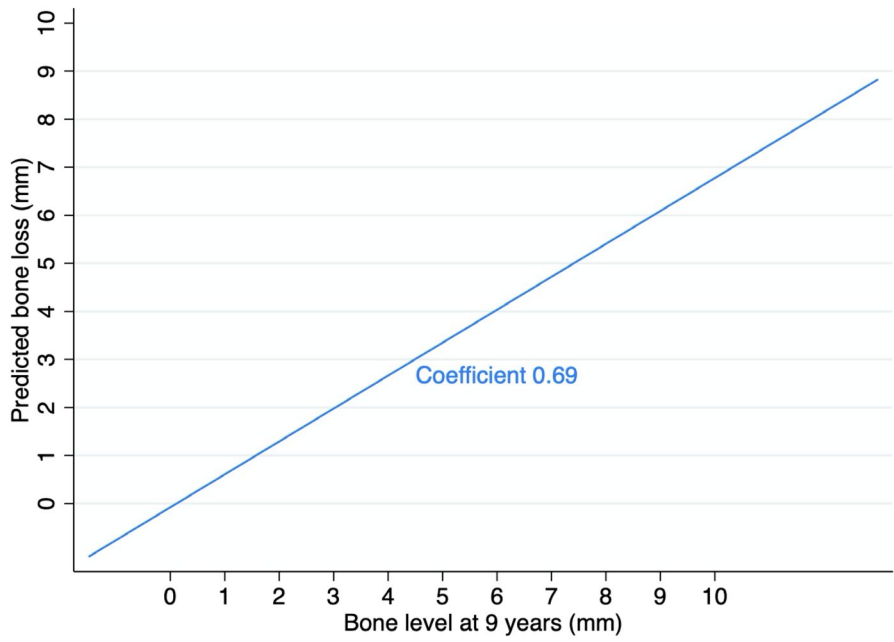**FIGURE A1** Assessment of bone levels and bone loss

FIGURE A2 Results of the multilevel linear regression analysis. Bone level at 9 years predicting bone loss
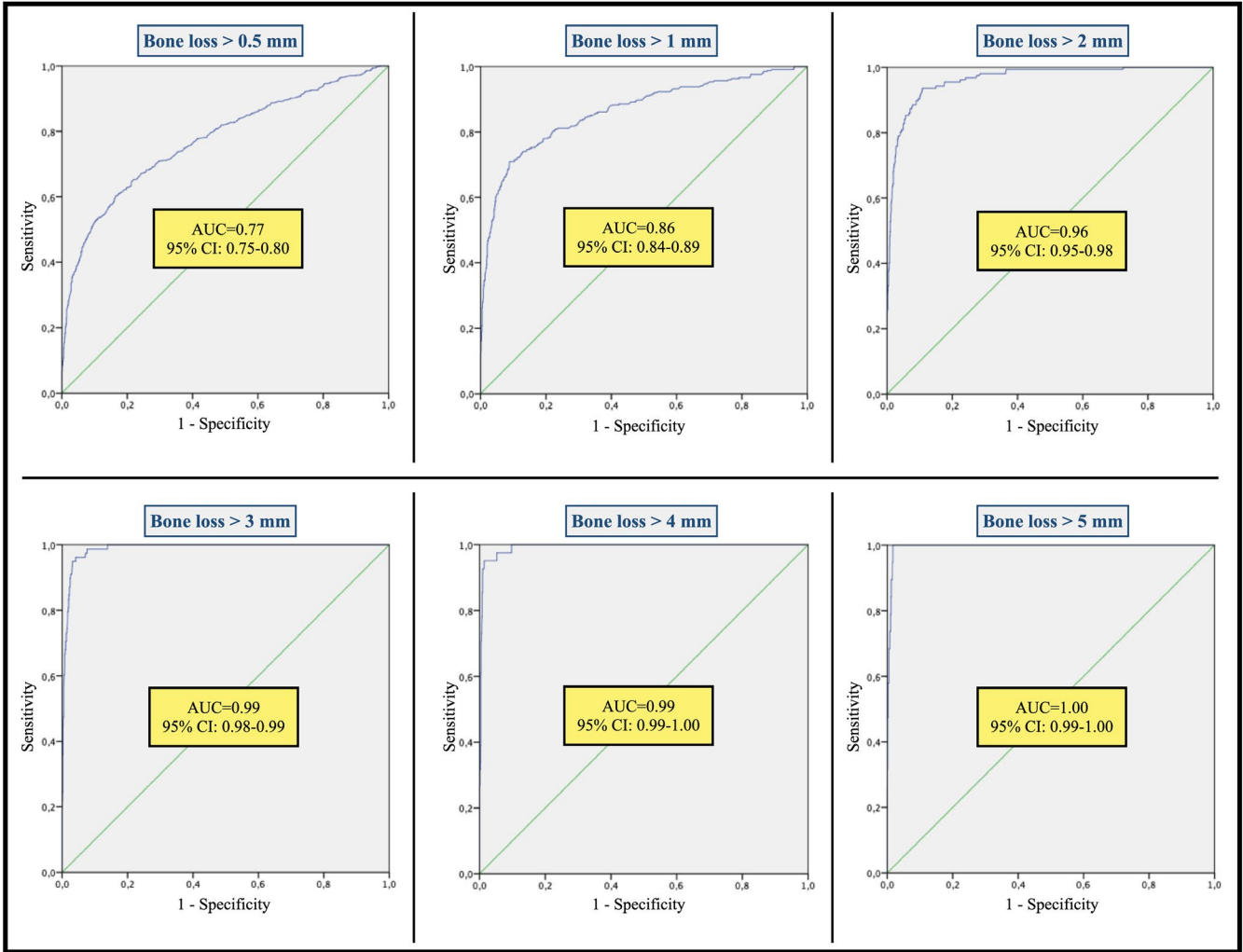
FIGURE A3 Receiver Operating Characteristic (ROC) curves for the detection of different quantities of radiographic bone loss using marginal bone levels at 9 years
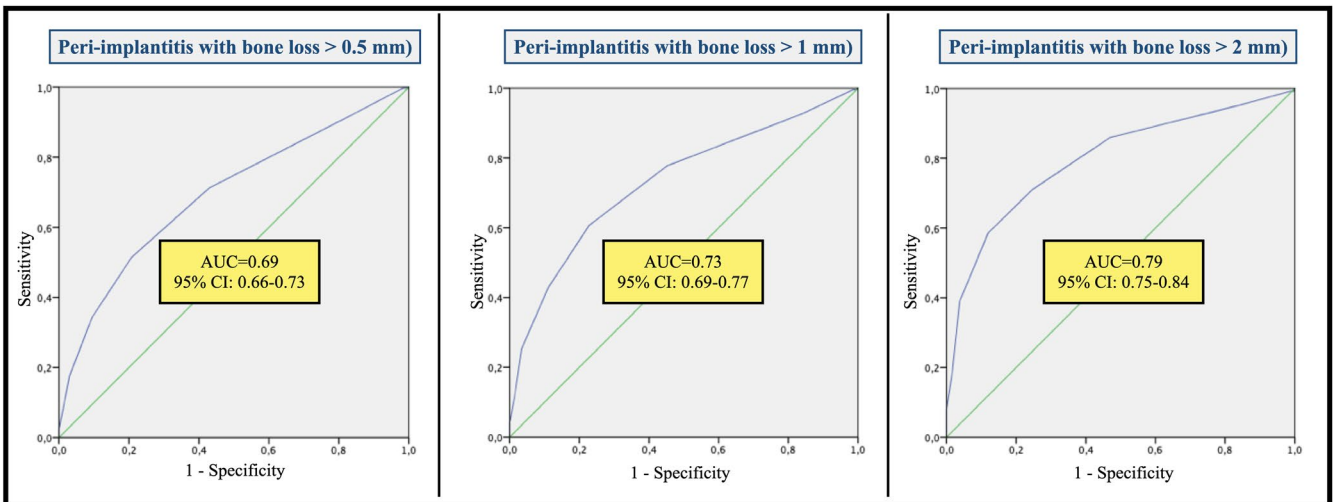
FIGURE A4 Receiver Operating Characteristic (ROC) curves for the detection of peri-implantitis (BoP/SoP & Bone loss > 0.5, >1, >2 mm) using PPD at 9 years

TABLE A1 Diagnostic accuracy of different thresholds of bone levels at 9 years for the detection of bone loss > 1 mm

Bone loss > 1 mm

	Bone level ≥ 0.5 mm	Bone level ≥ 1 mm	Bone level ≥ 1.5 mm	Bone level ≥ 2 mm	Bone level ≥ 2.5 mm	Bone level ≥ 3 mm	Bone level ≥ 3.5 mm	Bone level ≥ 4 mm	Bone level ≥ 4.5 mm	Bone level ≥ 5 mm
Prevalence% (95% CI)										20.5 (18.5–22.6)
Sensitivity%	93.2	84.5	74.9	65.3	49.2	38.4	30.7	21.7	15.2	13.0 (9.5–17.2)
(95% CI)	(89.9–95.7)	(80.1–88.3)	(69.8–79.6)	(59.9–70.5)	(43.6–54.8)	(33.1–43.9)	(25.7–36.0)	(17.3–26.6)	(11.4–19.6)	
Specificity%	41.0	67.5	84.6	92.9	97.0	98.3	99.1	99.5	99.8	99.9
(95% CI)	(38.3–43.8)	(64.8–70.1)	(82.5–86.6)	(91.3–94.3)	(95.9–97.8)	(97.5–99.0)	(98.4–99.6)	(99.0–99.8)	(99.4–100.0)	(99.6–100.0)
AUC (95% CI)	0.67	0.76	0.80	0.79	0.73	0.68	0.65	0.61	0.58	0.56
	(0.65–0.69)	(0.74–0.78)	(0.77–0.82)	(0.76–0.82)	(0.70–0.76)	(0.66–0.71)	(0.62–0.67)	(0.58–0.63)	(0.56–0.59)	(0.55–0.58)
PPV% (95% CI)	28.9	40.1	55.6	70.3	80.7	85.5	90.0	92.1	96.1	97.7 (87.7–99.9)
	(26.2–31.8)	(36.4–43.9)	(50.8–60.4)	(64.8–75.4)	(74.5–86.0)	(78.7–90.8)	(82.8–94.9)	(83.6–97.0)	(86.5–99.5)	
NPV% (95% CI)	95.9	94.4	92.9	91.2	88.1	86.1	84.7	83.1	82.0	81.7
	(93.9–97.4)	(92.7–95.8)	(91.3–94.3)	(89.5–92.7)	(86.3–89.8)	(84.2–87.9)	(82.8–86.5)	(81.2–85.0)	(80.0–83.9)	(79.7–83.6)

Abbreviations: AUC, Area under the curve; PPV, Positive predictive value; NPV, Negative predictive value

TABLE A2 Diagnostic accuracy of different clinical parameters for the detection of peri-implantitis with bone loss > 1 mm

Peri-implantitis (BoP/SoP+ & Bone loss > 1 mm)

Prevalence% (95% CI): 14.9 (13.2–16.8)

	BoP+ ≥1 site	BoP+ ≥3 sites	SoP+ ≥1 site	SoP+ ≥3 sites	BoP + or SoP+ ≥1 site	PPD ≥ 4 mm	PPD ≥ 5 mm	PPD ≥ 6 mm	PPD ≥ 7 mm	PPD ≥ 4 mm & BoP+ ≥1 site	PPD ≥ 5 mm & BoP+ ≥1 site	PPD ≥ 6 mm & BoP+ ≥1 site	PPD ≥ 7 mm & BoP+ ≥1 site
Sensitivity% (95% CI)	99.6 (97.7–100.0)	52.3 (45.7–58.9)	28.1 (22.4–34.3)	11.9 (8.1–16.8)	100.0 (98.4–100.0)	77.8 (71.9–82.9)	60.7 (54.1–67.0)	42.7 (36.3–49.3)	25.2 (19.8–31.3)	77.8 (71.9–82.9)	60.7 (54.1–67.0)	42.7 (36.3–49.3)	25.2 (19.8–31.3)
Specificity% (95% CI)	46.6 (44.0–49.4)	82.0 (79.9–84.1)	95.6 (94.4–96.6)	99.1 (98.4–99.5)	46.4 (43.7–49.1)	54.7 (52–57.5)	77.2 (74.8–79.4)	89.0 (87.1–90.6)	96.6 (95.4–97.5)	67.0 (64.4–69.6)	81.8 (79.6–83.9)	90.5 (88.7–92.0)	96.7 (95.6–97.6)
AUC (95% CI)	0.73 (0.72–0.75)	0.67 (0.64–0.71)	0.62 (0.59–0.65)	0.56 (0.53–0.58)	0.73 (0.72–0.75)	0.67 (0.63–0.69)	0.69 (0.66–0.72)	0.66 (0.63–0.69)	0.61 (0.58–0.64)	0.72 (0.69–0.75)	0.71 (0.68–0.75)	0.67 (0.63–0.70)	0.61 (0.58–0.64)
PPV% (95% CI)	24.6 (21.9–27.5)	33.9 (29.0–39.0)	52.8 (43.7–61.8)	70.0 (53.5–83.4)	24.6 (21.9–27.5)	23.8 (20.8–27.0)	32.6 (28.2–37.2)	41.3 (35.1–47.8)	57.1 (49.2–67.0)	30.0 (26.4–33.8)	37.8 (32.8–42.9)	44.8 (38.2–51.6)	58.4 (48.2–68.1)
NPV% (95% CI)	99.8 (99.1–100.0)	90.7 (89.0–92.3)	88.3 (86.6–89.9)	86.5 (84.7–88.2)	100.0 (99.4–100.0)	93.1 (91.1–94.8)	91.5 (89.7–93.1)	89.5 (87.7–91.2)	87.7 (85.8–89.3)	94.3 (92.6–95.7)	92.0 (90.2–93.5)	89.7 (87.9–91.3)	87.7 (85.9–89.3)

	PPD ≥ 4 mm & BoP+ ≥3 sites	PPD ≥ 5 mm & BoP+ ≥3 sites	PPD ≥ 6 mm & BoP+ ≥3 sites	PPD ≥ 7 mm & BoP+ ≥3 sites	PPD ≥ 4 mm & SoP+ ≥1 site	PPD ≥ 5 mm & SoP+ ≥1 site	PPD ≥ 6 mm & SoP+ ≥1 site	PPD ≥ 7 mm & SoP+ ≥1 site	PPD ≥ 4 mm & SoP+ ≥3 sites	PPD ≥ 5 mm & SoP+ ≥3 sites	PPD ≥ 6 mm & SoP+ ≥3 sites	PPD ≥ 7 mm & SoP+ ≥3 sites
Sensitivity% (95% CI)	47.4 (40.9–54.0)	42.3 (35.9–48.9)	33.8 (27.7–40.2)	21.8 (16.7–27.6)	26.9 (21.4–33.1)	25.6 (20.2–31.7)	20.1 (15.1–25.8)	15.0 (10.6–20.2)	77.8 (71.9–82.9)	60.7 (54.1–67.0)	42.7 (36.3–49.3)	-
Specificity% (95% CI)	86.6 (84.7–88.5)	90.8 (89.1–92.4)	94.6 (93.3–95.8)	97.9 (97.0–98.6)	95.6 (94.3–96.6)	96.0 (94.8–97.0)	97.0 (96.0–97.9)	98.8 (98.0–99.3)	66.9 (64.3–69.5)	81.8 (79.6–83.9)	90.5 (88.7–92.0)	-
AUC (95% CI)	0.67 (0.64–0.70)	0.67 (0.63–0.70)	0.64 (0.61–0.67)	0.60 (0.57–0.63)	0.61 (0.58–0.64)	0.61 (0.58–0.64)	0.59 (0.56–0.61)	0.57 (0.55–0.59)	0.72 (0.69–0.75)	0.71 (0.68–0.75)	0.67 (0.63–0.70)	-
PPV% (95% CI)	39.2 (33.5–45.2)	45.6 (38.9–52.5)	53.4 (45.0–61.6)	65.4 (53.8–75.8)	52.5 (43.2–61.7)	54.1 (44.3–63.6)	55.3 (44.1–66.1)	68.6 (54.1–80.9)	29.9 (26.3–33.7)	37.8 (32.8–42.9)	44.8 (38.2–51.6)	-
NPV% (95% CI)	90.1 (88.3–91.7)	89.7 (87.9–91.3)	88.7 (86.9–90.3)	87.3 (85.5–89.0)	87.8 (86.0–89.5)	87.7 (85.8–89.3)	87.0 (85.1–88.7)	86.5 (84.6–88.2)	94.3 (92.6–95.7)	92.0 (90.2–93.5)	89.7 (87.9–91.3)	-

Abbreviations: AUC, Area under the curve; PPV, Positive predictive value; NPV, Negative predictive value

TABLE A3 Diagnostic accuracy of different case definitions for the detection of peri-implantitis with bone loss > 1 mm in absence of baseline data

	Peri-implantitis (BoP/SoP+ & Bone loss > 1 mm)							
Prevalence% (95% CI)	14.9 (13.2–16.8)							
	Bone level ≥ 3 mm & BoP/SoP ≥ 1 site & PPD ≥ 6 mm (2017 WWP)	Bone level ≥ 2 mm & BoP/SoP ≥ 1 site (VIII EWP)	Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site	Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 4 mm	Bone level ≥ 1.5 mm & BoP/SoP ≥ 1 site & PPD ≥ 5 mm	Bone level ≥ 2 mm & BoP/SoP ≥ 1 site	Bone level ≥ 2 mm & BoP/SoP ≥ 1 site & PPD ≥ 4 mm	Bone level ≥ 2 mm & BoP/SoP ≥ 1 site & PPD ≥ 5 mm
Sensitivity % (95% CI)	24.7 (19.3–30.7)	67.7 (61.3–73.6)	77.4 (71.6–82.6)	63.4 (56.9–69.6)	51.1 (44.5–57.6)	67.7 (61.3–73.6)	56.2 (49.6–62.6)	46.0 (39.5–52.6)
Specificity % (95% CI)	99.4 (98.8–99.7)	96.1 (94.9–97.1)	91.4 (89.7–92.8)	94.0 (92.5–95.2)	96.0 (94.8–97.0)	96.1 (94.9–97.1)	97.2 (96.1–98.0)	97.7 (96.7–98.4)
AUC (95% CI)	0.62 (0.59–0.65)	0.82 (0.79–0.85)	0.84 (0.82–0.87)	0.79 (0.76–0.82)	0.74 (0.70–0.77)	0.82 (0.79–0.85)	0.77 (0.73–0.80)	0.72 (0.69–0.75)
PPV (95% CI)	87.9 (77.5–94.6)	75.4 (69.0–81.0)	61.1 (55.3–66.6)	64.8 (58.2–70.9)	69.0 (61.5–75.7)	75.4 (69.0–81.0)	77.6 (70.6–83.7)	77.7 (69.9–84.3)
NPV % (95% CI)	88.3 (86.5–89.9)	94.4 (93.1–95.6)	95.9 (94.6–96.9)	93.6 (92.2–94.9)	91.8 (90.2–93.2)	94.4 (93.1–95.6)	92.7 (91.2–94.0)	91.2 (89.6–92.6)

Abbreviations: AUC, Area under the curve; PPV, Positive predictive value; NPV, Negative predictive value