

Development and Internal Validation of a CBCT-Integrated Prognostic Nomogram for Tooth Survival in Periodontal-Endodontic Combined Lesions: A 5-Year Retrospective Cohort Study Running title: CBCT-integrated nomogram for tooth survival in perio-endo lesions

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Abstract

Aim

To identify clinical, CBCT-based radiographic, and patient-level predictors of 5-year tooth survival in periodontal-endodontic (perio-endo) combined lesions and develop an internally validated prognostic nomogram.

Methods

This retrospective cohort included 288 teeth from 288 patients with perio-endo combined lesions and ≥ 5 years of follow-up. Time to extraction was analysed using Kaplan–Meier estimation and multivariable Cox regression, with backward elimination from 14 candidate predictors. A points-based nomogram was developed from the final model. Discrimination was assessed using Harrell's C-index with 500 bootstrap resamples, and calibration compared predicted and observed 5-year survival across risk quintiles.

Results

Seventy-nine teeth (27.4%) were extracted, with a median time to extraction of 30 months. Overall 5-year survival was 72.6% (95% CI, 67.4–77.7%). Survival differed by lesion class, mobility, and furcation involvement. Independent predictors of extraction were inadequate root canal obturation (HR 2.41), greater mobility (HR 1.64 per grade), furcation involvement (HR 1.45 per grade), probing depth (HR 1.30/mm), CBCT volumetric bone loss (HR 1.0054/mm³), diabetes mellitus (HR 1.87), and poorer oral hygiene (HR 1.02/%). The nomogram showed good discrimination (apparent C-index 0.812; bootstrap-corrected 0.802) and close agreement between predicted and observed 5-year survival.

Conclusion

A CBCT-integrated nomogram combining seven clinical, radiographic, and patient-level variables provided accurate individualised prediction of 5-year tooth survival in perio-endo combined lesions. External validation is required before routine clinical implementation.

Clinical Relevance

Background: Prognosis in periodontal-endodontic (perio-endo) combined lesions is commonly based on individual clinical findings or conventional two-dimensional radiographs. These approaches do not integrate the multiple factors influencing whether a tooth can be successfully retained.

Added value of this study: This study developed an internally validated prognostic nomogram incorporating seven readily available predictors, including inadequate root canal obturation, mobility,

furcation involvement, probing depth, CBCT-derived volumetric bone loss, diabetes, and oral hygiene. The model provided good discrimination and calibration for predicting individual 5-year tooth survival.

Clinical implications: Integrating clinical, patient-level, and three-dimensional CBCT measurements may provide a more individualised estimate of prognosis than isolated risk factors. The nomogram could support chairside retain-versus-extract decisions and treatment planning for complex perio-endo lesions. External validation in independent and prospective populations is required before routine clinical use.

Introduction

Periodontal-endodontic (perio-endo) combined lesions arise from bidirectional communication between the pulpal and periodontal tissues through the apical foramen, lateral or accessory canals, or dentinal tubules, and constitute one of the most diagnostically and prognostically challenging presentations in restorative dentistry [1, 4, 24]. Since Simon, Glick and Frank first proposed a mechanistic classification of endodontic-periodontal lesions in 1972 [1], subsequent systems, including the Al-Fouzan modification [2] and the more recent European Federation of Periodontology consensus classification and overview reviews [5, 6], have refined the diagnostic categorisation of these lesions into primary endodontic, primary periodontal, true combined and retrograde subtypes. However, classification systems describe lesion origin and clinical presentation; they offer limited individualised, quantitative guidance on the probability that a specific tooth will survive over the medium to long term [3, 6].

Existing retrospective studies of perio-endo lesions have generally reported prognostic factors such as tooth mobility, probing depth, furcation involvement and quality of root canal treatment individually, or through simple univariable comparisons, without integrating them into a single, clinically deployable risk-estimation instrument [7, 8, 9]. Furthermore, the great majority of prior prognostic work has relied on two-dimensional periapical radiography, a projection technique that systematically underestimates the true extent of alveolar bone loss, furcation involvement and root morphology relative to cone-beam computed tomography (CBCT) [10, 11, 16]. CBCT is now widely available in specialist periodontic and endodontic practice and permits volumetric, three-dimensional quantification of bone defects that cannot be obtained from planar radiographs [10, 11, 12].

Prognostic nomograms - graphical or tabular point-scoring systems derived from multivariable regression models - are now well established in oncology and cardiology as tools that translate a complex regression equation into an individualised probability estimate that a clinician can apply chairside without specialised software [36, 37, 38]. Analogous nomograms have not yet been developed for perio-endo combined lesions, despite the fact that the retain-versus-extract decision in these lesions is frequently made under considerable prognostic uncertainty, with direct consequences for treatment planning, cost, and patient counselling regarding implant alternatives [3, 7].

Well-validated ordinal and binary classification systems already exist for several of the candidate predictors relevant to perio-endo prognosis, including the Miller classification of tooth mobility [17] and the Glickman and Hamp-Nyman-Lindhe classifications of furcation involvement [18, 19], and substantial

evidence links the quality of root canal obturation to endodontic treatment outcome [20, 21, 22, 23]. Patient-level factors such as smoking, diabetes mellitus, oral hygiene and periodontal maintenance compliance are independently associated with tooth loss in periodontally compromised dentitions [25, 26, 27], and machine-learning and classical statistical approaches alike have begun to be applied to tooth-loss prediction in general periodontitis populations [15], but not specifically to perio-endo combined lesions with CBCT-derived predictors.

The novel contribution of the present study relative to prior descriptive prognostic-factor studies is threefold: (i) incorporation of CBCT-based volumetric bone loss and furcation bone-loss depth, rather than two-dimensional periapical estimates alone, as quantitative predictors; (ii) construction of a multivariable Cox regression-based nomogram integrating clinical, radiographic and patient-level factors into a single numerical tooth-survival probability score, rather than reporting isolated risk factors in isolation; and (iii) internal validation of the nomogram's discrimination (Harrell's C-index) and calibration using bootstrap resampling, following contemporary methodological guidance for prediction-model development [31, 32, 33, 34, 35]. The primary objective of this study was therefore to identify independent clinical, radiographic and patient-level prognostic factors for 5-year tooth survival in perio-endo combined lesions and to develop a multivariable prognostic nomogram; secondary objectives were to internally validate the nomogram, to describe changes in probing depth, clinical attachment level and CBCT-measured bone fill among surviving teeth, and to compare survival between Simon-Glick-Frank lesion classes.

Methods

Study design and setting

This was a retrospective cohort study with survival analysis and nomogram development, conducted using archived clinical, periodontal charting and CBCT imaging records from the periodontics and endodontics departments of a dental teaching hospital. Patients treated 5–7 years before study initiation were eligible, so as to allow a minimum 5-year follow-up window for every included tooth. Institutional Review Board / Research Ethics Committee approval was obtained prior to chart and CBCT data extraction. Because the study constituted a retrospective review of existing, de-identified clinical and radiographic records, a waiver of individual informed consent was granted. All clinical data and CBCT images were anonymised and stored securely, accessible only to the research team, in accordance with local data-protection regulations and the principles of the Declaration of Helsinki.

Participants

Eligible teeth had a diagnosis of a perio-endo combined lesion confirmed by clinical and radiographic/CBCT criteria at baseline, had completed combined periodontal and endodontic treatment, had a minimum of 5 years of documented follow-up (recall visits and radiographs), and had baseline

CBCT imaging available. Teeth with a vertical root fracture at baseline, teeth requiring extraction for non-periodontal/non-endodontic reasons (e.g., orthodontic or prosthetic indications), teeth with incomplete baseline or follow-up records, and patients with uncontrolled systemic disease precluding periodontal maintenance therapy were excluded. Each tooth was drawn from a distinct patient (one index tooth per patient), so no clustering adjustment for repeated observations within patients was required. The final analytic cohort comprised 288 teeth. Sample size had been set a priori at 300–350 teeth, anticipating 80–100 extraction events at an approximate 25–30% 5-year extraction rate, so as to provide at least 10 events per candidate predictor variable for the Cox model, following established events-per-variable guidance for regression-based prediction models [29, 30, 31]; the achieved cohort of 288 teeth with 79 extraction events approximated this target.

CBCT protocol and radiographic assessment

CBCT protocol and radiographic assessment

Baseline CBCT volumes were acquired as part of routine diagnostic work-up for suspected perio-endo combined lesions and were re-analysed by calibrated examiners blinded to the eventual tooth-survival outcome, using multiplanar reconstruction protocols consistent with published guidance on CBCT applications in periodontics and endodontics [10, 11, 12]. From each CBCT volume, volumetric bone loss (mm³) around the affected tooth was quantified, together with the depth of furcation bone loss (mm) on multiplanar reconstructions, the pattern of bone loss (horizontal, vertical or combined) and the presence of accessory/lateral canals or complex root morphology [24]. These CBCT-derived measures were combined with two-dimensional clinical periodontal parameters (probing depth, clinical attachment level) recorded at the deepest site around each tooth.

Variables and definitions

Patient-level variables comprised age, sex, diabetes mellitus status, smoking status (never/former/current), oral hygiene (O'Leary plaque index, %) and periodontal maintenance compliance (proportion of scheduled recall visits attended, %). Tooth/clinical variables comprised FDI tooth number, Simon-Glick-Frank lesion classification (true combined, retrograde periodontal, retrograde endodontic), baseline probing depth and clinical attachment level (deepest site, mm), Miller tooth-mobility grade (0–3) [17], Glickman furcation-involvement grade (0–4) [18, 19], and quality of root canal obturation (adequate/inadequate) [20, 21, 22, 23]. CBCT-based radiographic variables comprised volumetric bone loss (mm³) [10, 11], bone-loss pattern, presence of accessory canals/complex root morphology [24], and furcation bone-loss depth (mm). Outcome variables, ascertained at the 5-year follow-up point, comprised tooth survival status (survived/extracted), time to extraction in months where applicable, and probing depth, clinical attachment level and CBCT bone fill at final follow-up for surviving teeth.

The primary outcome for survival analysis was time to tooth extraction. Follow-up time was defined as the time from baseline treatment to extraction for teeth that were extracted, and as 60 months (the 5-

year inclusion criterion) for teeth that survived to their final documented follow-up, which were treated as right-censored at 60 months. Teeth extracted for reasons unrelated to periodontal or endodontic failure had already been excluded at the eligibility stage, so all recorded extractions represented perio-endo-related treatment failure.

Statistical analysis

Baseline characteristics were summarised as median (interquartile range) for continuous variables and n (%) for categorical variables, and were compared between survived and extracted teeth using the Mann-Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. Kaplan-Meier estimation was used to describe overall and stratum-specific 5-year tooth-survival curves (stratified by lesion classification, tooth mobility grade, furcation grade, and RCT obturation quality), with between-stratum comparison by the log-rank test.

Multivariable Cox proportional hazards regression was used to identify independent predictors of extraction. Fourteen candidate predictors specified in the study protocol (age, diabetes mellitus, smoking status, oral hygiene index, maintenance compliance, lesion classification, baseline probing depth, baseline clinical attachment level, tooth mobility, furcation involvement, RCT obturation quality, CBCT volumetric bone loss, bone-loss pattern, and furcation bone-loss depth) were entered into a full model, and a parsimonious final model was derived by manual backward elimination, sequentially removing the term with the largest Wald P value (threshold $P > 0.10$) until all retained terms reached $P < 0.10$. The proportional-hazards assumption was assessed for the final model using Schoenfeld residuals, correlating scaled residuals for each covariate with event time.

A points-based nomogram was constructed from the final Cox model using standard linear-rescaling logic [36, 37, 38]: for each predictor, the product of its regression coefficient (log hazard ratio) and its observed range in the cohort ('risk range') was calculated; the predictor with the largest risk range was assigned a 0-100-point scale, and all other predictors were scaled proportionally to this anchor, yielding points per unit increase for each covariate. Total points across all seven predictors were then mapped back to a predicted 5-year survival probability using the model's baseline cumulative hazard at 60 months (Breslow estimator).

Discrimination of the final model was quantified using Harrell's concordance index (C-index), computed manually over all usable (comparable) pairs of teeth, with pairs consisting of a shorter documented event time and a longer time (event or censored) counted as concordant if the tooth with the shorter time also had the higher model-predicted risk [28, 38]. Internal validation used 500 bootstrap resamples (sampling with replacement, $n = 288$ per resample): the model was refitted in each bootstrap sample, its C-index evaluated both in the bootstrap sample and in the original cohort, and the average difference (optimism) was subtracted from the apparent C-index to obtain an optimism-corrected estimate [34, 35]. Calibration was assessed by grouping teeth into quintiles of nomogram-predicted 5-year survival and comparing the mean predicted probability in each quintile with the corresponding Kaplan-Meier

observed 5-year survival; this comparison was repeated across 500 (predicted-vs-observed point estimate) and 300 (calibration-curve overlay) bootstrap resamples to characterise sampling variability of the calibration relationship, following recommended bootstrap calibration methodology [34, 35].

Changes in probing depth, clinical attachment level and CBCT bone fill among surviving teeth between baseline and final follow-up were compared using the Wilcoxon signed-rank test. All statistical analyses were performed in Python (pandas, numpy, scipy.stats and statsmodels, including the SurvfuncRight and PHReg implementations for Kaplan-Meier estimation and Cox regression, respectively); a two-sided $P < 0.05$ was considered statistically significant throughout.

Ethical considerations

Approval was obtained from the dental hospital's Institutional Review Board / Research Ethics Committee prior to chart and CBCT data extraction. As this was a retrospective review of existing, de-identified clinical and radiographic records, a waiver of individual informed consent was granted by the Committee. All clinical data and CBCT images were anonymised prior to analysis and stored securely, with access restricted to the research team, in accordance with local data-protection regulations and the Declaration of Helsinki.

Results

Cohort characteristics and baseline comparison

A total of 288 teeth from 288 patients met all eligibility criteria and were included in the analytic cohort. Median patient age was 53.7 years (SD 11.5; range 24-82), 158 patients (54.9%) were female, and 41 (14.2%) had diabetes mellitus. Median oral hygiene index was 32.2% (SD 12.7) and median periodontal maintenance compliance was 70.6% (SD 18.4). Lesion classification was true combined in 125 teeth (43.4%), retrograde periodontal in 99 (34.4%) and retrograde endodontic in 64 (22.2%).

Seventy-nine teeth (27.4%) were extracted during the 5-year observation period, at a median time to extraction of 30 months (interquartile range, 16-43 months); the remaining 209 teeth (72.6%) survived to their final documented 5-year follow-up and were censored at 60 months. Table 1 compares baseline characteristics between teeth that survived and teeth that were subsequently extracted. Extracted teeth had significantly greater baseline probing depth (median 9 vs 7 mm, $P < 0.001$), greater baseline clinical attachment level (median 11 vs 9 mm, $P < 0.001$), greater CBCT volumetric bone loss (median 203 vs 131 mm³, $P < 0.001$), and greater furcation bone-loss depth (median 2.5 vs 0.8 mm, $P < 0.001$) than teeth that survived. Extracted teeth were also more likely to present with true combined lesions (59.5% vs 37.3%, $P = 0.003$), higher Miller mobility grades and higher Glickman furcation grades (both $P < 0.001$). Age, sex, diabetes mellitus, smoking status, oral hygiene index, maintenance compliance, RCT obturation quality, bone-loss pattern and presence of an accessory canal did not differ significantly between groups at the $P < 0.05$ threshold in unadjusted comparison, although inadequate RCT obturation was numerically more frequent among extracted teeth (51.9% vs 39.7%, $P = 0.083$).

Table 1. Baseline characteristics of teeth that survived versus teeth that were extracted over 5 years of follow-up.

Variable	Survived (n=209)	Extracted (n=79)	P value
Age (years), median (IQR)	53.0 (45.0-61.0)	54.0 (47.0-62.5)	0.875
Sex, male, n (%)	90 (43.1%)	40 (50.6%)	0.289
Diabetes mellitus, n (%)	28 (13.4%)	13 (16.5%)	0.571
Smoking status, n (%)			0.373
Never	99 (47.4%)	36 (45.6%)	
Former	57 (27.3%)	17 (21.5%)	
Current	53 (25.4%)	26 (32.9%)	
Oral hygiene index (O'Leary, %), median (IQR)	31.7 (23.5-40.7)	31.9 (23.9-44.0)	0.511
Maintenance compliance (%), median (IQR)	71.0 (57.0-86.0)	69.0 (53.5-82.5)	0.356
Lesion classification, n (%)			0.003
True combined	78 (37.3%)	47 (59.5%)	
Retrograde periodontal	79 (37.8%)	20 (25.3%)	
Retrograde endodontic	52 (24.9%)	12 (15.2%)	
Baseline probing depth (mm), median (IQR)	7.0 (6.0-8.0)	9.0 (8.0-10.0)	<0.001
Baseline clinical attachment level (mm), median (IQR)	9.0 (7.0-10.0)	11.0 (9.0-12.0)	<0.001
Tooth mobility (Miller grade), n (%)			<0.001
Grade 0	74 (35.4%)	11 (13.9%)	
Grade 1	82 (39.2%)	18 (22.8%)	
Grade 2	42 (20.1%)	32 (40.5%)	
Grade 3	11 (5.3%)	18 (22.8%)	
Furcation involvement (Glickman grade), n (%)			<0.001
Grade 0	100 (47.8%)	13 (16.5%)	
Grade 1	51 (24.4%)	14 (17.7%)	
Grade 2	42 (20.1%)	24 (30.4%)	
Grade 3	13 (6.2%)	19 (24.1%)	
Grade 4	3 (1.4%)	9 (11.4%)	
RCT obturation quality, n (%)			0.083

Variable	Survived (n=209)	Extracted (n=79)	P value
Adequate	126 (60.3%)	38 (48.1%)	
Inadequate	83 (39.7%)	41 (51.9%)	
CBCT volumetric bone loss (mm ³), median (IQR)	131.0 (94.0-181.0)	203.0 (155.0-243.0)	<0.001
Bone loss pattern, n (%)			0.261
Horizontal	88 (42.1%)	25 (31.6%)	
Vertical	56 (26.8%)	26 (32.9%)	
Combined	65 (31.1%)	28 (35.4%)	
Accessory canal present, n (%)	71 (34.0%)	32 (40.5%)	0.336
Furcation bone loss depth (mm, CBCT), median (IQR)	0.8 (0.0-2.1)	2.5 (1.2-3.9)	<0.001

Abbreviations: CAL, clinical attachment level; CBCT, cone-beam computed tomography; IQR, interquartile range; RCT, root canal treatment. P values from Mann-Whitney U test (continuous variables) or chi-square/Fisher's exact test (categorical variables).

<>Kaplan-Meier survival analysis

Overall 5-year Kaplan-Meier tooth survival for the cohort was 72.6% (95% CI, 67.4-77.7%) (Fig. 1). Five-year survival differed significantly according to Simon-Glick-Frank lesion classification (log-rank chi-square=11.9, P=0.003): retrograde endodontic lesions had the most favourable 5-year survival (81.2%, 95% CI 71.7-90.8%), followed by retrograde periodontal lesions (79.8%, 95% CI 71.9-87.7%), while true combined lesions had the lowest 5-year survival (62.4%, 95% CI 53.9-70.9%) (Fig. 2).

Five-year survival decreased progressively with increasing furcation involvement, from 88.5% (95% CI 82.6-94.4%) in furcation grade 0 to 78.5% (68.5-88.5%) in grade 1, 63.6% (52.0-75.2%) in grade 2, 40.6% (23.6-57.6%) in grade 3, and 25.0% (0.5-49.5%) in grade 4 (log-rank chi-square=54.9, P<0.001; Fig. 3). A similar dose-response gradient was observed for Miller mobility grade, from 87.1% (79.9-94.2%) in grade 0 to 82.0% (74.5-89.5%) in grade 1, 56.8% (45.5-68.0%) in grade 2, and 37.9% (20.3-55.6%) in grade 3 (log-rank chi-square=48.5, P<0.001). Five-year survival was higher for teeth with adequate RCT obturation than inadequate obturation (76.8%, 95% CI 70.4-83.3%, vs 66.9%, 58.7-75.2%; log-rank chi-square=4.3, P=0.039), whereas bone-loss pattern (horizontal, vertical or combined) was not significantly associated with survival in unadjusted analysis (log-rank chi-square=2.6, P=0.279).

Multivariable Cox regression

In the full multivariable Cox model containing all 14 candidate predictors, tooth mobility (HR 1.77 per grade, 95% CI 1.35-2.30, $P<0.001$), inadequate RCT obturation (HR 2.20, 1.34-3.62, $P=0.002$), CBCT volumetric bone loss (HR 1.0073/mm³, 1.0033-1.0113, $P<0.001$) and diabetes mellitus (HR 2.19, 1.12-4.28, $P=0.022$) were independently associated with extraction, while age, baseline probing depth, baseline clinical attachment level, furcation involvement, furcation bone-loss depth, maintenance compliance, oral hygiene index, lesion classification and bone-loss pattern did not reach significance once all covariates were mutually adjusted, reflecting collinearity among several of the correlated clinical and radiographic severity measures.

Backward elimination (removal threshold, Wald $P>0.10$) yielded a final seven-predictor model retaining diabetes mellitus, oral hygiene index, baseline probing depth, tooth mobility, furcation involvement, RCT obturation quality and CBCT volumetric bone loss (Table S1, Fig. 4). In this final model, inadequate RCT obturation carried the largest point-estimate hazard ratio for extraction (HR 2.41, 95% CI 1.52-3.82, $P<0.001$), followed by diabetes mellitus (HR 1.87, 0.99-3.52, $P=0.054$), tooth mobility (HR 1.64 per Miller grade, 1.26-2.13, $P<0.001$), furcation involvement (HR 1.45 per Glickman grade, 1.19-1.76, $P<0.001$), baseline probing depth (HR 1.30/mm, 1.11-1.53, $P=0.001$), CBCT volumetric bone loss (HR 1.0054/mm³, 1.0017-1.0092, $P=0.004$; equivalent to HR approximately 1.72 per additional 100 mm³ of bone loss), and oral hygiene index (HR 1.02/percentage point, 1.00-1.04, $P=0.060$). Schoenfeld-residual testing of the final model showed no significant time-dependence for six of the seven retained covariates (all $P>0.10$); furcation involvement showed a statistically significant correlation with time ($r=0.295$, $P=0.008$), suggesting a degree of non-proportionality in its hazard over the follow-up period, which is discussed further below.

Nomogram construction

A points-based nomogram was derived from the final seven-predictor Cox model (Table S2). Points were assigned to each predictor in proportion to its regression coefficient and its observed range in the cohort, with baseline probing depth (range 4-13 mm) anchoring the 0-100-point scale because it contributed the largest risk range among the retained predictors. On this scale, inadequate RCT obturation contributed 36.9 points (versus 0 for adequate obturation), diabetes mellitus contributed 26.2 points, maximal tooth mobility (grade 3) contributed 62.0 points, maximal furcation involvement (grade 4) contributed 62.1 points, baseline probing depth of 12 mm contributed 88.9 points, an oral hygiene index of 70% contributed 48.5 points, and a CBCT volumetric bone loss of 300 mm³ contributed 63.7 points. Summed across all seven predictors, total nomogram points for an individual tooth ranged from approximately 0 (most favourable combination of predictors) to approximately 410 (least favourable combination); total points were converted to a predicted 5-year survival probability using the model's estimated baseline survival function (Table S2b). A tooth accumulating 100 total points corresponded to an estimated 5-year survival probability of approximately 95%, whereas a tooth accumulating 250 points corresponded to an estimated 5-year survival probability of approximately 16%, illustrating the steep, clinically discriminating transition in predicted risk across the middle of the points scale.

Discrimination and calibration

The final Cox model showed good apparent discrimination, with an apparent Harrell's C-index of 0.812. Following internal validation with 500 bootstrap resamples, the mean optimism (difference between bootstrap-sample and original-sample concordance) was 0.010, yielding an optimism-corrected (bootstrap-validated) C-index of 0.802, indicating limited overfitting and good expected discrimination in new data drawn from a similar population.

Calibration was assessed by comparing nomogram-predicted and Kaplan-Meier-observed 5-year survival across predicted-risk quintiles (Table S3, Fig. 5). Agreement between predicted and observed survival was close across the full range of predicted risk: in the lowest-survival quintile, mean predicted 5-year survival was 26.6% against a Kaplan-Meier-observed survival of 24.1% (95% CI 13.1-35.2%); in the highest-survival quintile, mean predicted survival was 97.0% against an observed survival of 94.8% (95% CI 89.1-100%). The bootstrap-resampled calibration curve (500 resamples for point estimates; 300 resamples for the overlaid calibration cloud) tracked closely to the 45-degree line of perfect calibration across the full predicted-probability range, with only slight overestimation of survival in the mid-risk range (Fig. 5).

Secondary outcomes: clinical and radiographic change among surviving teeth

Among the 209 teeth that survived to 5-year follow-up, probing depth decreased from a baseline median of 7 mm (IQR 6-8) to 6 mm (IQR 5-7) at final follow-up (mean reduction 1.3 mm, SD 0.7; Wilcoxon signed-rank $P < 0.001$), and clinical attachment level improved from a baseline median of 9 mm (IQR 7-10) to 8 mm (IQR 6-10) (mean gain 0.8 mm, SD 0.7; $P < 0.001$). CBCT-quantified bone fill at final follow-up averaged 21.6 mm³ (SD 12.4), corresponding to partial fill of approximately 20% of the baseline volumetric bone-loss defect on average, consistent with the expected pattern of measurable but incomplete radiographic bone fill following successful combined periodontal-endodontic therapy over a 5-year window.

Fig. 6 illustrates the relationship between baseline probing depth and CBCT volumetric bone loss, stratified by 5-year outcome. Extracted teeth (red) clustered towards the upper right of the plot, reflecting the combination of deeper baseline pockets and greater volumetric bone loss identified as independent predictors in the multivariable model, although considerable overlap between outcome groups was evident at intermediate probing depths (7-9 mm), underscoring the rationale for a multivariable, rather than single-variable, prognostic approach.

Discussion

Principal findings

In this retrospective cohort of 288 teeth with perio-endo combined lesions and a minimum of 5 years of documented follow-up, overall tooth survival was 72.6%, with 27.4% of teeth extracted at a median of 30

months. Seven independent predictors of extraction were identified in the final multivariable Cox model - inadequate root canal (RCT) obturation, tooth mobility, furcation involvement, baseline probing depth, CBCT-quantified volumetric bone loss, diabetes mellitus, and oral hygiene index - which together underpinned a points-based nomogram with good apparent discrimination (Harrell's C-index 0.812) that was well preserved after bootstrap internal validation (optimism-corrected C-index 0.802) and showed close agreement between predicted and Kaplan-Meier-observed 5-year survival across the full range of predicted risk. To our knowledge, this is among the first studies to integrate CBCT-derived volumetric and morphometric measurements with clinical and patient-level variables into a single Cox regression-based nomogram specifically for perio-endo combined lesions, rather than reporting these factors as isolated, unweighted risk indicators.

Comparison with prior perio-endo prognostic literature

The overall 5-year survival observed here (72.6%) sits within, albeit towards the lower end of, the range reported in prior retrospective cohorts of treated endodontic-periodontal lesions, which have generally reported survival between roughly 70% and 90% depending on lesion severity, follow-up duration and the proportion of true combined lesions in the sample [7,8,9]. The markedly poorer prognosis of true combined lesions relative to retrograde periodontal or retrograde endodontic lesions in the present cohort (62.4% vs 79.8% vs 81.2% 5-year survival, respectively) is consistent with the pathophysiological expectation that lesions with a genuinely combined periodontal-pulpal aetiology reflect more advanced, bidirectional tissue destruction than lesions that are predominantly unidirectional in origin, and mirrors the ordering of prognosis reported in earlier classification-based cohort analyses [1,2,3,9]. Our finding that tooth mobility and furcation involvement showed a clear dose-response relationship with extraction risk, with 5-year survival falling from approximately 87-89% in the absence of mobility or furcation involvement to well under 40% at the highest grades, closely parallels the prognostic gradients reported in periodontally compromised, non-perio-endo cohorts followed for 10 to 18 years [13,14,25,26], reinforcing the generalisability of these two clinical signs as prognostic anchors across periodontal disease subtypes.

The independent association between inadequate RCT obturation and extraction (hazard ratio 2.41) is consistent with a substantial endodontic outcomes literature linking obturation quality and length to periapical healing and long-term tooth retention [20,21,22,23]; in the context of perio-endo combined lesions specifically, this finding underscores that endodontic treatment quality is not merely a co-therapy consideration but an independently weighted determinant of survival, of comparable or greater prognostic weight than the periodontal severity indices in our final model. The persistence of a diabetes mellitus effect (hazard ratio 1.87, of borderline significance) after adjustment for local disease severity is in keeping with evidence that systemic glycaemic status modulates periodontal wound healing and disease progression independently of local factors [27], while the comparatively modest, borderline effect of oral hygiene index in the adjusted model, despite its established univariable association with

periodontal outcomes generally, likely reflects at least partial mediation of oral hygiene's effect through the probing depth, mobility and furcation covariates that were simultaneously included in the model.

CBCT versus two-dimensional radiography

A central premise of this study was that CBCT-derived volumetric and morphometric measurements would add prognostic information beyond what could be obtained from two-dimensional periapical radiography. CBCT volumetric bone loss remained an independent predictor of extraction after adjustment for clinical probing depth and attachment level, indicating that it captures dimensions of bone destruction - particularly in the buccolingual and interradicular planes - that are not fully reflected in mesiodistal periapical projections or single-site probing measurements, consistent with prior comparative imaging literature demonstrating that CBCT more accurately quantifies alveolar bone loss and furcation involvement than periapical or panoramic radiography, which are prone to superimposition artefact and geometric distortion [10,11,12,16]. This is clinically relevant because furcation and interradicular bone defects are frequently under-diagnosed or under-staged on two-dimensional imaging, potentially leading to an overly optimistic prognosis being assigned to a tooth whose true three-dimensional bone support is more compromised than it appears radiographically [11,12]. The present findings support the incorporation of CBCT-based volumetric and morphometric measures as a distinct, non-redundant prognostic axis, complementary to rather than a replacement for careful clinical periodontal charting.

Clinical utility of the nomogram for the retain-versus-extract decision

The clinical value of a nomogram lies in its capacity to translate a multivariable statistical model into a bedside or chairside tool that a clinician can apply without specialised software, a principle well established in oncological prognostication [36,37]. In the present nomogram, a tooth accumulating around 100 total points corresponded to an estimated 95% probability of 5-year survival, while a tooth accumulating around 250 points corresponded to an estimated survival probability of only around 16%, illustrating a steep, clinically actionable transition in predicted risk across the middle of the scale. In practical terms, a tooth with adequate RCT obturation, Miller grade 0-1 mobility, Glickman grade 0-1 furcation involvement, and moderate CBCT volumetric bone loss would fall towards the low-point, high-survival end of the nomogram and would reasonably support a decision to proceed with combined non-surgical or surgical periodontal-endodontic therapy with a favourable prognosis; conversely, a tooth combining inadequate obturation, grade 3 mobility, and grade 3-4 furcation involvement would accumulate points placing it in a range associated with a markedly reduced 5-year survival probability, which may support earlier discussion of extraction and implant or prosthetic planning with the patient, avoiding repeated, resource-intensive but low-yield attempts at tooth retention. Because all seven nomogram inputs are obtainable from a single clinical examination plus a diagnostic CBCT scan already

indicated for suspected perio-endo pathology, the tool imposes no additional data-collection burden beyond standard specialist work-up.

Strengths

This study has several methodological strengths. First, it integrates CBCT-derived volumetric and morphometric measurements, rather than two-dimensional radiographic estimates, into a formal multivariable survival model, addressing a specific evidence gap identified in prior perio-endo prognostic literature [3,9]. Second, the sample size (288 teeth, 79 extraction events) approximated the pre-specified target derived from established events-per-variable heuristics for Cox regression [29,30,31], supporting reasonably stable coefficient estimation once the model was reduced from 14 candidate predictors to a parsimonious seven-predictor final model by backward elimination. Third, internal validation followed contemporary methodological recommendations, combining Harrell's C-index for discrimination with 500-resample bootstrap optimism correction and bootstrap-resampled calibration assessment across predicted-risk quintiles, in line with guidance for the development and internal validation of clinical prediction models [32,33,34,35]. Fourth, the nomogram construction method used a transparent, reproducible linear-rescaling approach directly traceable back to the underlying Cox coefficients, so that the point allocations in Table S2 can be independently reconstructed or updated as new data accrue.

Limitations

Several limitations should be considered when interpreting these findings. First, the retrospective design is subject to variability in recall intervals, documentation completeness, and potential misclassification of lesion type or extraction indication across the study period; although CBCT re-measurement was performed by calibrated examiners blinded to outcome to mitigate this, residual measurement variability cannot be excluded, particularly as CBCT acquisition protocols and voxel resolution may have varied slightly over the multi-year recruitment window. Second, although the achieved sample approximated the pre-specified target, the number of extraction events ($n=79$) relative to the 14 originally specified candidate predictors fell somewhat short of the conventional 10-events-per-variable heuristic for the full model [29,30], which is one reason a parsimonious final model was derived by backward elimination rather than reporting the full 14-predictor model as the basis for the nomogram; nonetheless, backward elimination itself can introduce selection instability in modest-sized datasets, and the borderline hazard ratios for diabetes mellitus and oral hygiene index (both with confidence intervals spanning or closely approaching unity) should be interpreted with appropriate caution. Third, Schoenfeld residual testing indicated a statistically significant time-dependence for the furcation involvement covariate, suggesting that its hazard for extraction may not be strictly constant over the 5-year follow-up window (for example, if furcation-related extractions cluster disproportionately in either the early or late follow-up period); this represents a mild violation of the proportional hazards assumption for one of seven model covariates, and future iterations of the nomogram could consider a time-varying coefficient or restricted mean

survival time formulation for this variable. Fourth, this study reports internal validation only; the bootstrap-corrected C-index and calibration curves describe expected performance on data drawn from the same underlying population and sampling process, but do not establish transportability to other institutions, populations, examiners, or CBCT hardware, which requires formal external validation. Fifth, the CBCT-based measurements, while more accurate than two-dimensional radiography, still carry inherent measurement error related to voxel size, scatter and beam-hardening artefact, and the volumetric bone-loss metric used here summarises a complex three-dimensional defect into a single number, which may obscure prognostically relevant differences in defect morphology (for example, contained versus non-contained defects) that a purely volumetric measure cannot capture. Finally, as in any observational cohort, unmeasured confounding (for example, variation in operator experience, specific surgical or regenerative techniques used, or prosthetic loading of the tooth) cannot be excluded as a contributor to the observed associations.

Future directions

Prospective, multicentre validation of this nomogram in independent cohorts, ideally with standardised CBCT acquisition protocols, is the logical next step before clinical deployment, following the TRIPOD framework for prediction-model reporting and validation [32,33]. Future work should also examine whether incorporation of a time-varying formulation for furcation involvement improves calibration in the later follow-up period, whether regenerative periodontal or endodontic microsurgical techniques modify the hazard associated with individual predictors, and whether integration of the nomogram into a simple digital calculator or CBCT-viewer plug-in improves its uptake and reproducibility in routine specialist practice. Extension of the follow-up period beyond 5 years, and formal cost-effectiveness comparison of nomogram-guided retention versus early extraction and implant placement, would further strengthen the clinical case for this type of tool in perio-endo combined lesions.

Conclusion

In this 5-year retrospective cohort of periodontal-endodontic combined lesions, inadequate root canal obturation, tooth mobility, furcation involvement, baseline probing depth, CBCT-quantified volumetric bone loss, diabetes mellitus and oral hygiene index were identified as independent predictors of tooth extraction. A points-based nomogram integrating these seven clinical, radiographic and patient-level variables achieved good discrimination (bootstrap-corrected Harrell's C-index, 0.802) and good calibration against Kaplan-Meier-observed 5-year survival across the full range of predicted risk. By combining routinely obtainable clinical findings with CBCT measurements already acquired as part of standard diagnostic work-up, this nomogram offers a practical, chairside decision-support tool to help clinicians and patients weigh the probability of long-term tooth survival against the alternative of extraction and implant or prosthetic rehabilitation. External validation in independent cohorts is required before the tool can be recommended for routine clinical deployment.

Declarations

Acknowledgments

None declared

Conflict of Interest

None declared

Source of Funding

None declared

Ethics Approval:

Institutional Review Board / Research Ethics Committee approval was obtained prior to chart and CBCT data extraction.

The study was approved by the Institutional Review Board (IRB) / Research Ethics Committee (REC) prior to the extraction of chart and CBCT data.

Informed Consent:

Because the study constituted a retrospective review of existing, de-identified clinical and radiographic records, a waiver of individual informed consent was granted.

Data Availability: Available from the corresponding author upon reasonable request

Consent for publication: not applicable.

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Figures

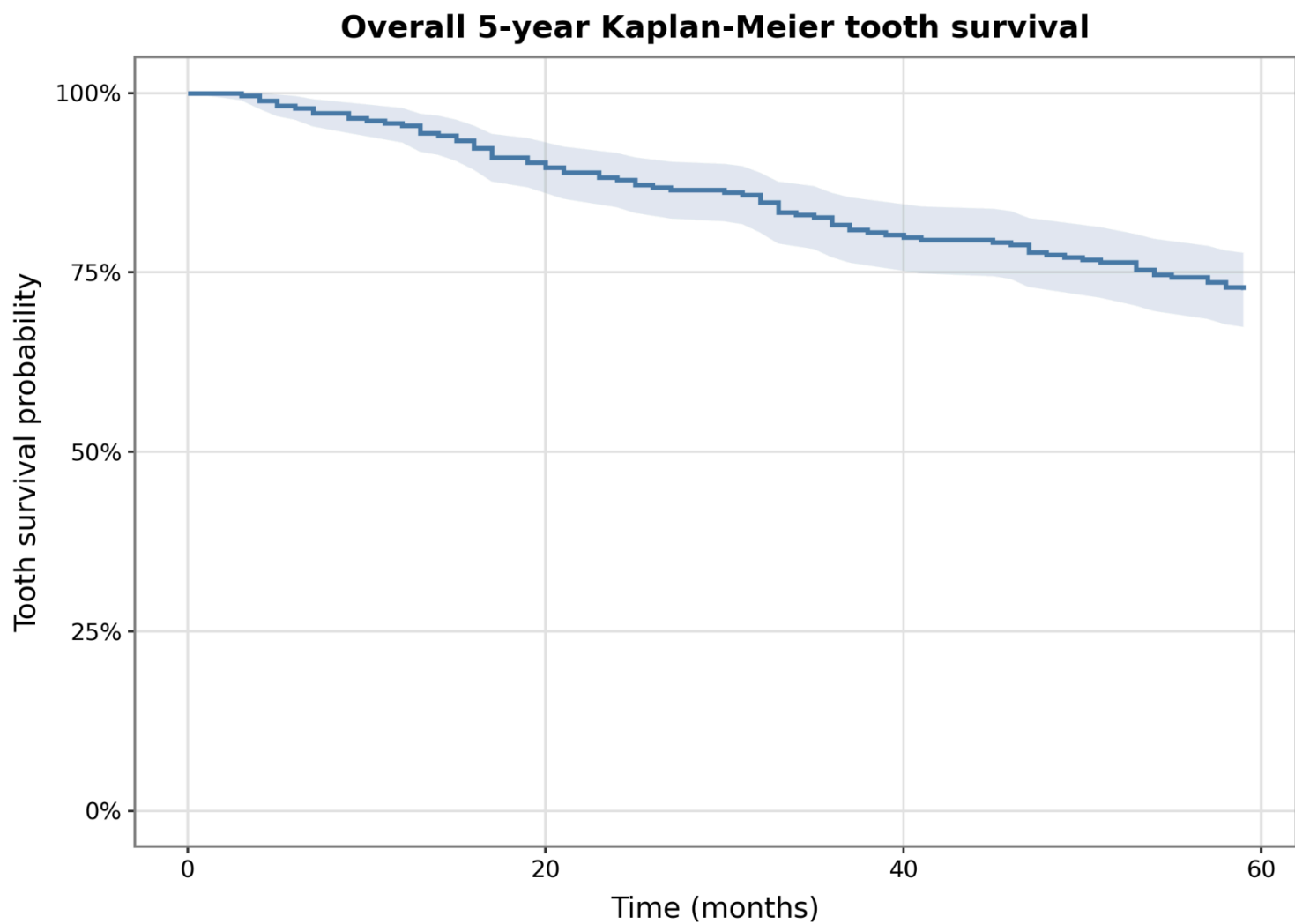


Figure 1

Overall Kaplan-Meier tooth-survival curve for the 5-year cohort (n=288; shaded band, 95% pointwise confidence interval).

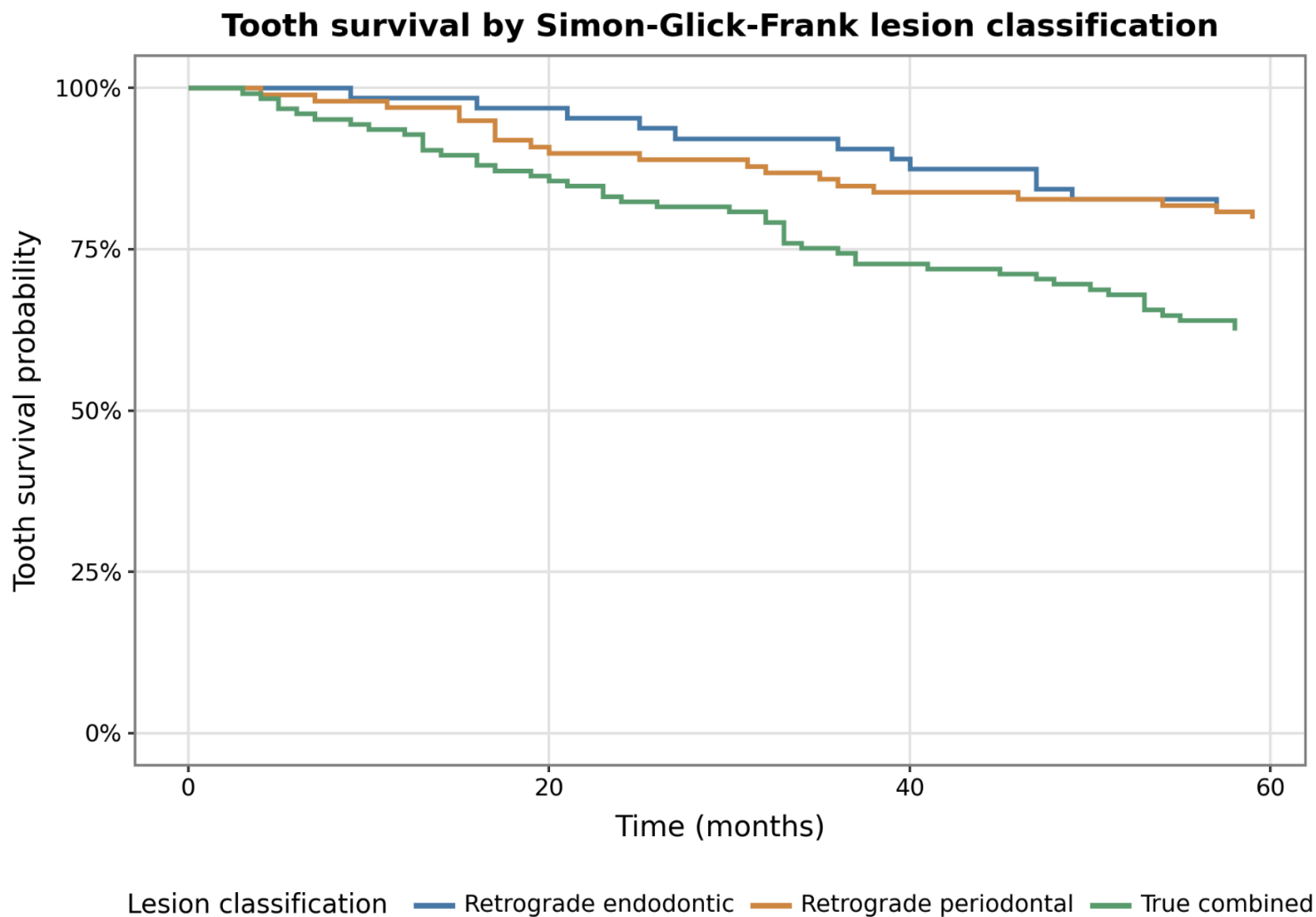


Figure 2

Kaplan-Meier tooth-survival curves stratified by Simon-Glick-Frank lesion classification (log-rank chi-square=11.9, $P=0.003$).

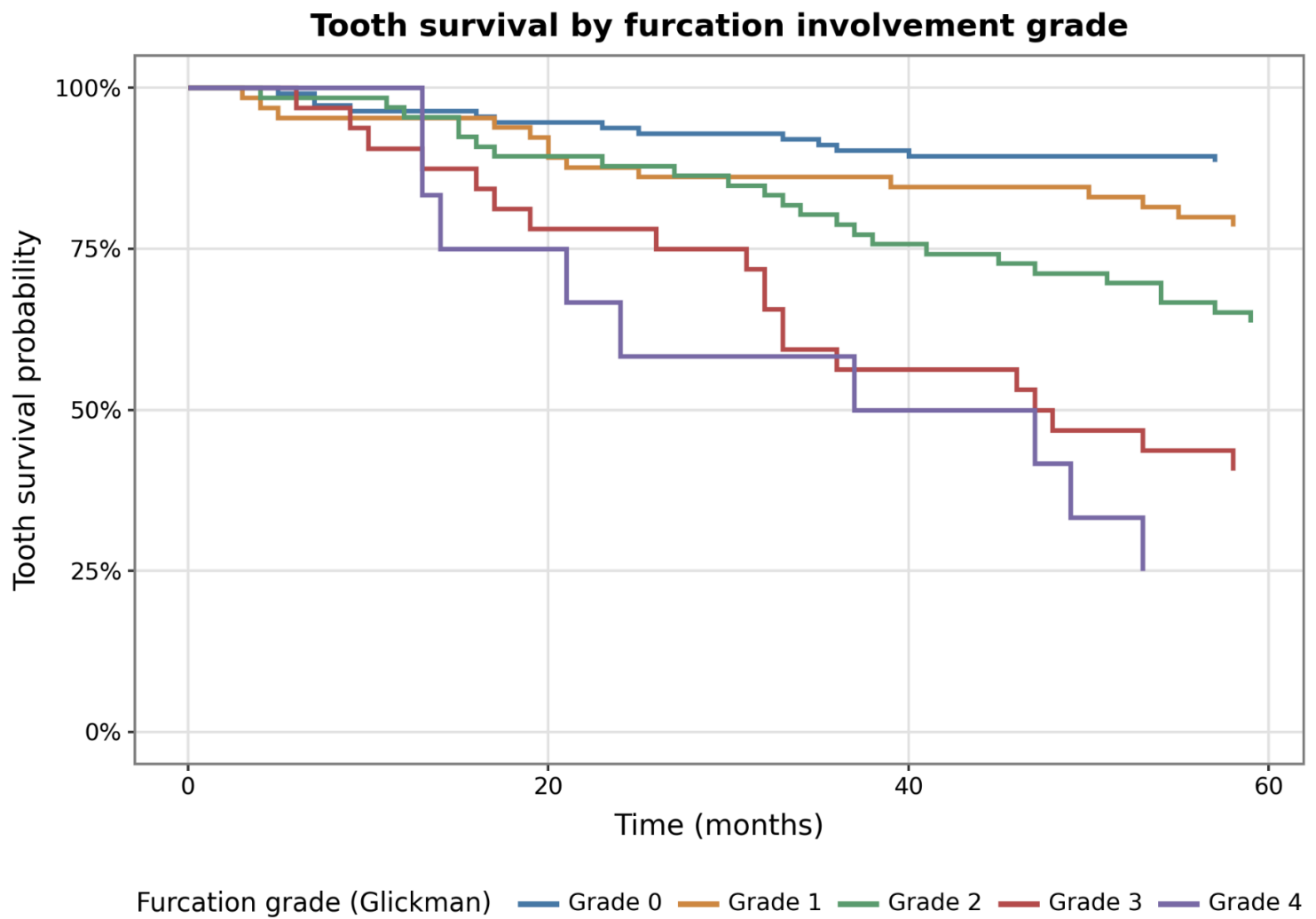


Figure 3

Kaplan-Meier tooth-survival curves stratified by Glickman furcation-involvement grade (log-rank chi-square=54.9, $P<0.001$).

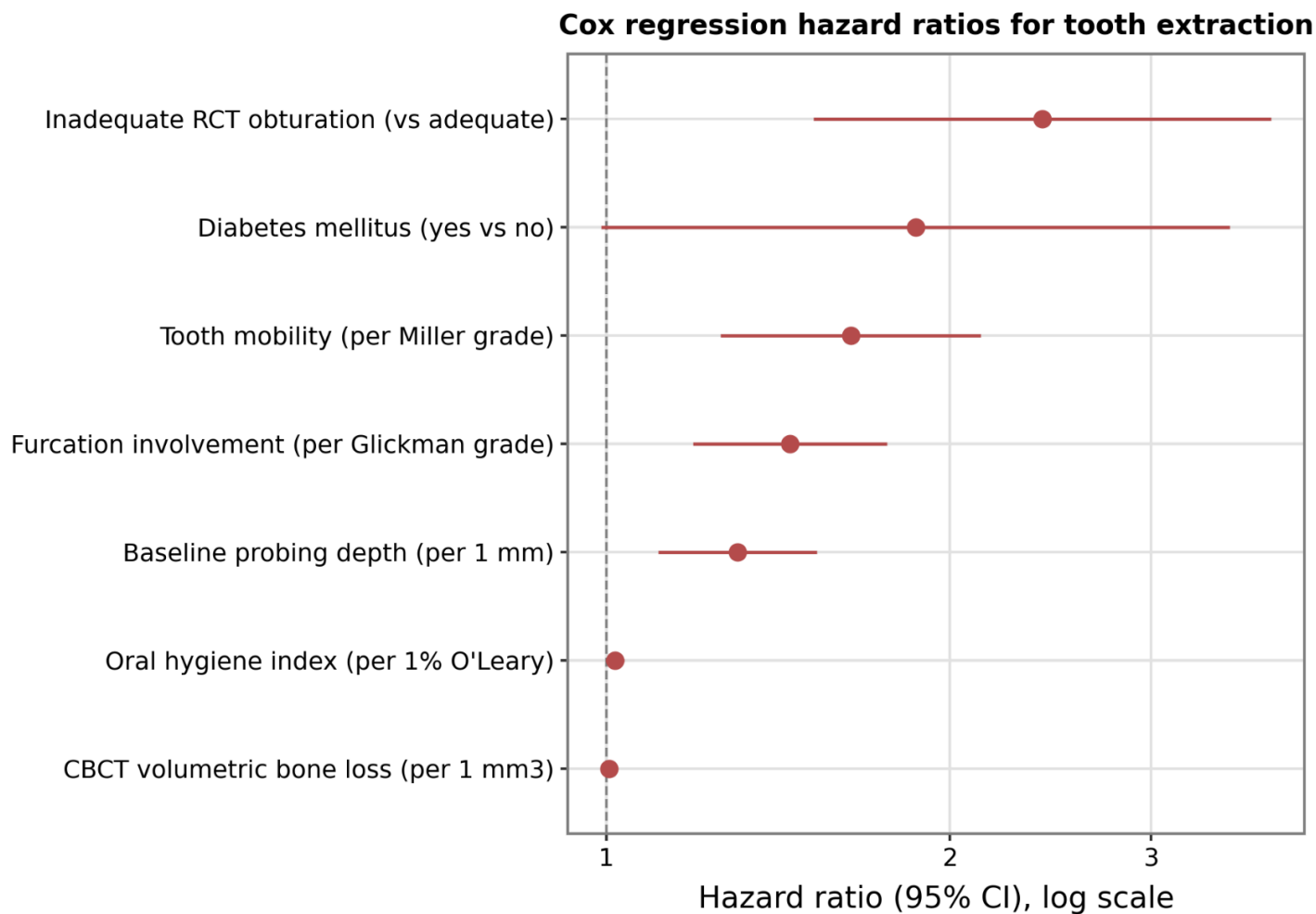


Figure 4

Forest plot of hazard ratios (95% CI) from the final multivariable Cox regression model for tooth extraction.

Bootstrap-resampled calibration of the nomogram (500 resamples)

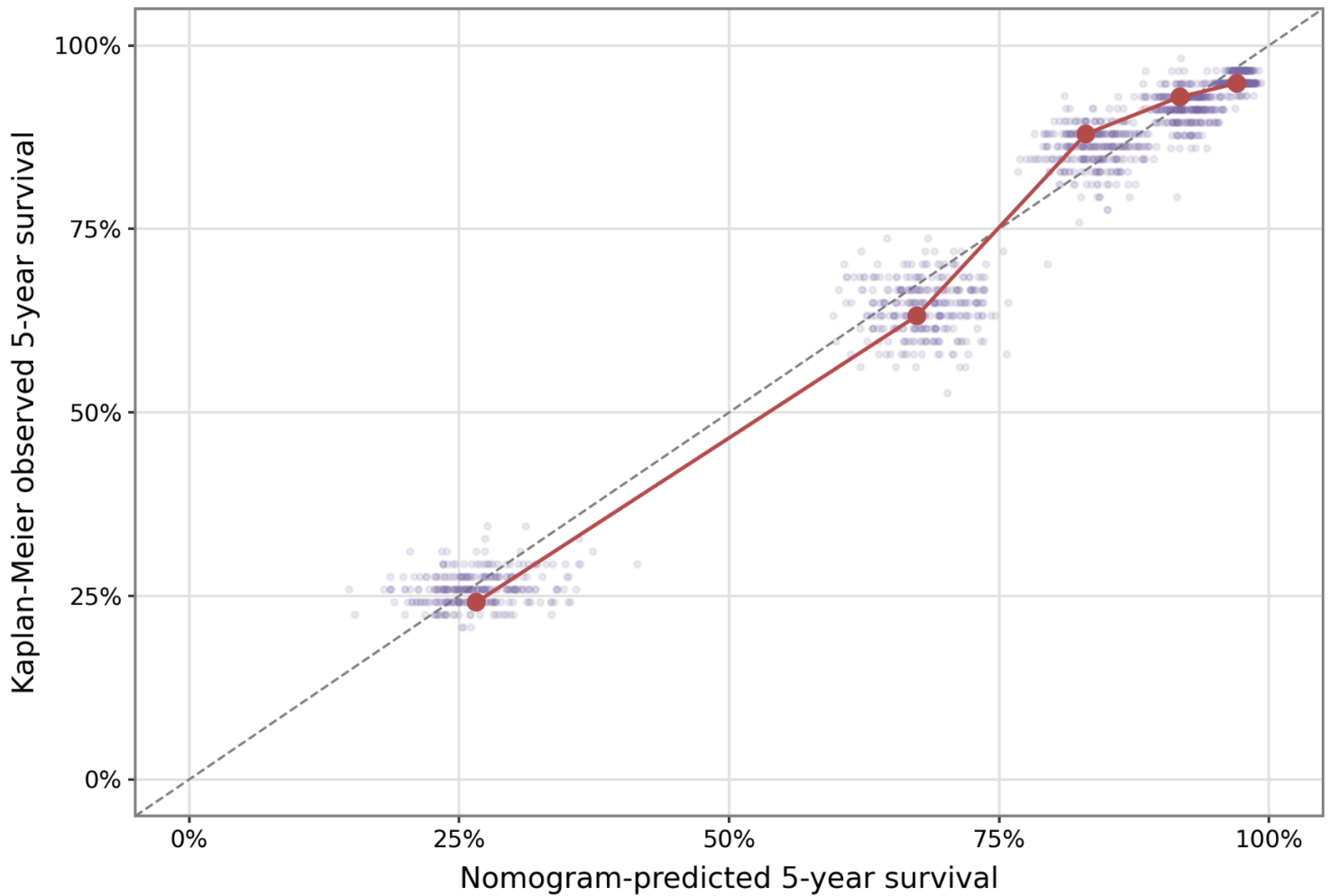


Figure 5

Bootstrap-resampled calibration plot of nomogram-predicted versus Kaplan-Meier-observed 5-year tooth survival (500 resamples for quintile point estimates, overlaid with 300 bootstrap calibration replicates; dashed line, ideal calibration).

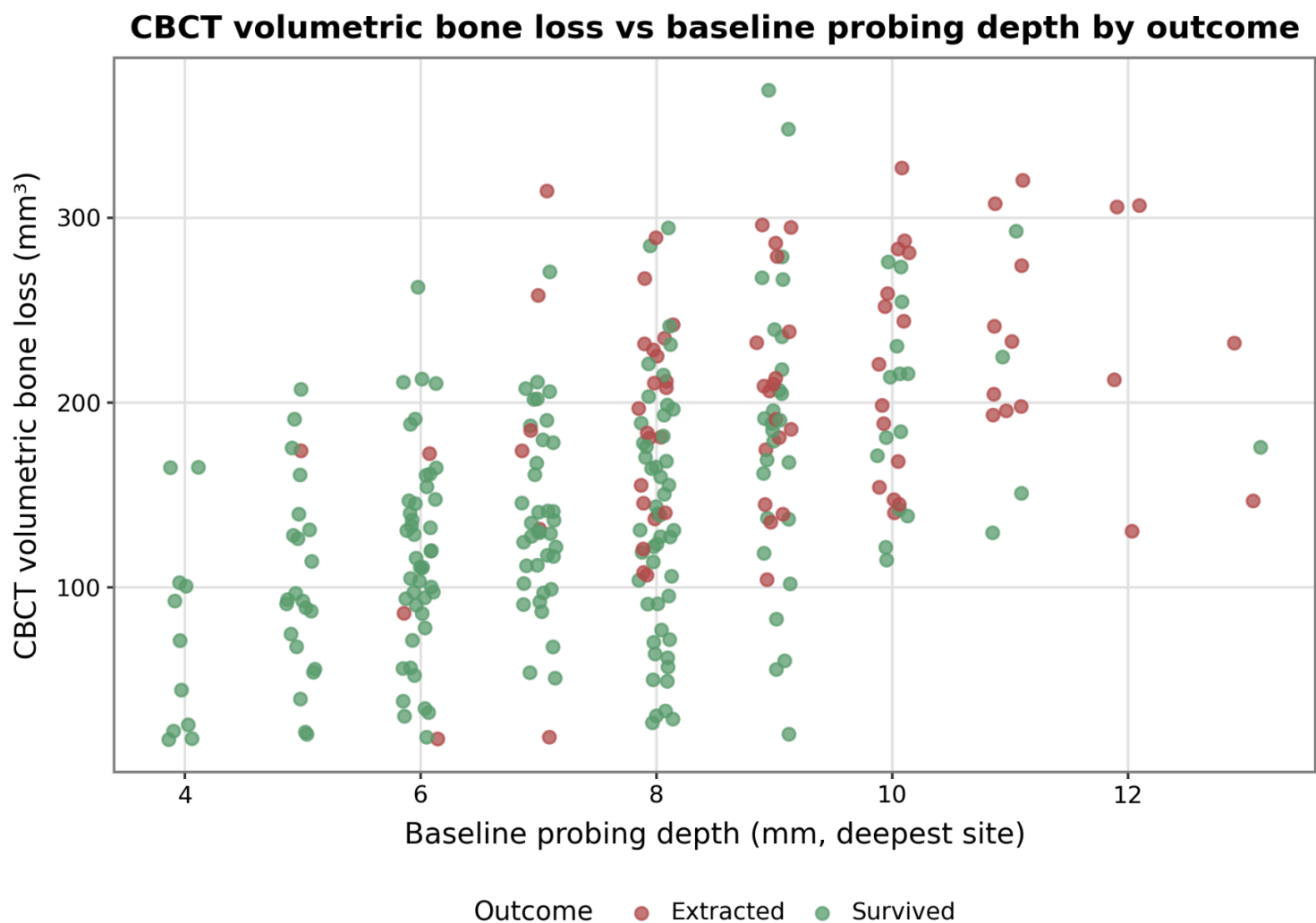


Figure 6

Scatter plot of CBCT-quantified volumetric bone loss versus baseline probing depth, coloured by 5-year outcome (survived vs extracted).

Supplementary Files

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- [SuppTables.docx](#)