Journal of Dental Sciences

Volume 21 | Issue 2 Article 56

2026

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Journal of Dental Sciences 21 (2026) 1148–1155

Available online at https://jds.ads.org.tw/journal/

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Original Article

Graph neural network-based prediction of all-cause and cardiovascular mortality using periodontal site-level data from National Health and Nutrition Examination Survey (NHANES)

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Received 23 November 2025; Final revision received 26 December 2025
Available online ■ ■ ■

KEYWORDS
Periodontitis;
Graph neural network;
Site-level periodontal data;
NHANES;
All-cause mortality;
Cardiovascular mortality

Abstract *Background/purpose:* Periodontitis is a common chronic inflammatory disease linked to systemic conditions. We applied a graph convolutional network (GCN) to site-level periodontal data to predict all-cause and cardiovascular mortality from National Health and Nutrition Examination Survey (NHANES).
Materials and methods: Adults aged ≥30 years with full-mouth periodontal exams and linked mortality data through December 31, 2019 were included. Periodontal probing depth and clinical loss of attachment were measured. Each chart was converted into a graph with 168 nodes and anatomically defined edges. Graph-level embeddings were combined with age and sex to predict mortality. Model performance was evaluated in an independent test set using receiver operating characteristic - area under the curve (ROC AUC) and precision-recall - area under the curve (PR AUC).
Results: Among 9034 participants (1000 deaths), deceased individuals had significantly greater mean probing depth (1.71 ± 0.68 mm vs. 1.58 ± 0.66 mm) and loss of attachment (2.46 ± 1.34 mm vs. 1.86 ± 1.06 mm) than survivors (both $P < 0.001$). Adjusted mortality probabilities rose from 2.2 % to 5.6 % across probing depth quartiles and from 2.2 % to 6.3 % across attachment loss quartiles. The GCN achieved strong discrimination, with ROC AUC = 0.831 and 0.845 and PR AUC = 0.397 and 0.203 for all-cause and cardiovascular mortality, respectively.

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https://doi.org/10.1016/j.jds.2025.12.027

Conclusion: A GCN applied to site-level periodontal data achieved strong discrimination in predicting mortality. This finding highlights the prognostic significance of periodontal health and demonstrates the potential of graph-based deep learning for modeling complex periodontal–systemic interactions.

Introduction

Periodontitis is a chronic inflammatory disease of the supporting tissues of teeth that can result in progressive clinical attachment and bone loss. It also remains one of the leading causes of tooth loss worldwide. It is highly prevalent, affecting a substantial proportion of adults across all regions and contributing significantly to the global burden of oral disease.[1] A recent systematic review and meta-analysis estimated that between 2011 and 2020, the prevalence of periodontitis in dentate adults was approximately 62 %, with severe periodontitis affecting nearly one quarter.[2] These findings underscore that periodontitis is not only a dental problem but also a major public health concern.

Beyond its impact on oral function and quality of life, periodontitis has been increasingly recognized as a contributor to systemic health outcomes. Evidences from epidemiological and mechanistic studies links periodontitis with cardiovascular disease, diabetes, respiratory disease, and mortality.[1,3,4] The biological pathways proposed include systemic dissemination of periodontal pathogens, recurrent bacteremia, and the chronic low-grade inflammation leading to endothelial dysfunction and atherosclerosis.[3–5] Elevated inflammatory mediators, such as C-reactive protein and interleukin-6, observed in patients with periodontitis, support these systemic links.

Several large cohort studies have demonstrated the associations between periodontitis and all-cause or cause-specific mortality.[6–14] Collectively, these findings suggest that the presence and severity of periodontitis could carry important prognostic implications beyond oral health. Despite these advances, most prior studies have summarized periodontal disease using categorical definitions or composite indices, such as the Centers for Disease Control and Prevention/American Academy of Periodontology (CDC/AAP) case definition. While these approaches are practical for population-level analyses, they fail to capture the heterogeneity and spatial distribution of disease across the dentition.[9,12] For instance, localized clusters of deep periodontal pockets in posterior sextants may have different systemic implications compared with generalized shallow attachment loss, yet such distinctions are lost in aggregated indices. This represents a critical gap in the literature, as spatial disease patterns may provide additional prognostic value.

Recent developments in artificial intelligence provide new opportunities to overcome these limitations. Graph neural networks (GNNs) are designed to model complex relational structures in non-Euclidean data, allowing integration of both node-level attributes and their interconnections. They have shown strong performance in biomedical applications, including risk prediction using electronic health records and multimodal clinical data.[15,16]

In this study, we applied a graph convolutional network (GCN) to site-level periodontal data from the National Health and Nutrition Examination Survey (NHANES) 2011–2014. Each periodontal site was represented as a node containing probing depth and clinical attachment loss, with edges reflecting anatomical adjacency across the dentition. Our objective was to determine whether this graph-based deep learning approach could improve prediction of all-cause and cardiovascular mortality. We hypothesized that the GCN would capture clinically meaningful spatial patterns of periodontitis and provide prognostic insights beyond traditional case definitions.

Materials and methods

Study population

Data were obtained from NHANES 2011–2014, a nationally representative cross-sectional survey of the U.S. civilian, non-institutionalized population conducted by the National Center for Health Statistics. Adults aged ≥30 years who underwent a full-mouth periodontal examination and had linked mortality data available from the National Death Index (NDI) were eligible for inclusion. Mortality status and cause of death were determined through follow-up until December 31, 2019. Participants with incomplete periodontal data (N = 4766) or missing mortality information (N = 936) were excluded, yielding a final analytic sample of 9034 participants (Fig. 1). From the 9034 participants, a subset of 7651 dentate participants with sufficient site-level features was utilized for the GNN model. This dataset was then partitioned into training (N = 5355), validation (N = 1148), and testing (N = 1148) sets.

Outcomes

Mortality outcomes were derived from the NHANES public-use linked mortality files. The primary outcome was all-cause mortality, defined as death from any cause during the follow-up period. The secondary outcome was cardiovascular mortality, defined as death with an underlying cause attributed to diseases of the circulatory system, in accordance with the National Center for Health Statistics leading cause of death classification. Specifically, participants whose leading cause of death was coded in the

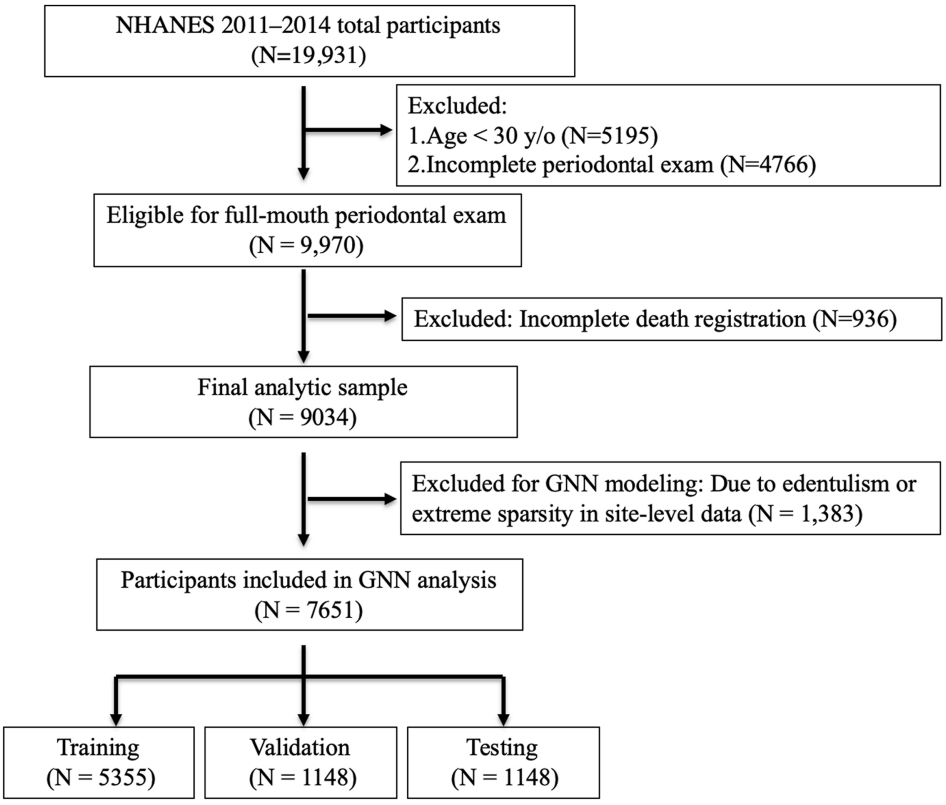

Figure 1 Flowchart of study participant selection.

UCOD_LEADING variable as "Diseases of Heart" or "Cerebrovascular Diseases" were classified as cardiovascular deaths. Binary indicators were created for each outcome, coded as 1 for participants who died and 0 for those who survived during follow-up.

Periodontal examination

Periodontal examinations were performed by trained and calibrated examiners using a manual periodontal probe according to standardized NHANES protocols. Probing depth (PD) and clinical loss of attachment (LOA) were measured at six sites per tooth: mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual. Third molars were excluded, resulting in up to 28 teeth and 168 site-level measurements per participant. Examiner calibration was conducted periodically to ensure consistency and accuracy across survey cycles.

Graph representation of periodontal data

Each participant's periodontal examination was transformed into a graph to preserve the anatomical and spatial complexity of the dentition. Each periodontal site was represented as a node with probing depth and clinical loss of attachment as quantitative node features. Anatomical adjacency defined the edges: within each tooth, mesial and distal sites were connected to buccal and lingual counterparts to reflect intra-tooth continuity, and neighboring teeth were connected mesially and distally to represent proximal contacts within the same dental arch. This design created a connected graph that captured both localized disease severity and broader spatial patterns across the dentition. To account for missing site measurements, a binary indicator was added to the node feature set, enabling the model to learn whether missingness itself carried prognostic information.

Graph neural network model

We implemented a GNN based on a GCN architecture. Each participant was represented as a graph with up to 168 nodes, corresponding to periodontal sites assessed in the NHANES full-mouth periodontal examination. Node-level features included probing depth, clinical loss of attachment, and a binary indicator of missingness. Edges reflected anatomical adjacency, preserving the spatial structure of the dentition. The GCN consisted of three stacked graph convolutional layers (GCNConv), each followed by rectified linear unit (ReLU) activation and dropout for regularization. Graph-level embeddings were derived through global mean pooling across nodes. Demographic covariates (age and sex) were processed in parallel through a linear layer, and the resulting embedding was concatenated with the pooled graph representation. The combined feature vector was passed through a fully connected layer to produce probability estimates for all-cause and cardiovascular mortality. Model training was performed using cross-entropy loss with the Adam optimizer.

Model training and evaluation

The analytic sample was randomly partitioned into training, validation, and testing sets with stratification by mortality outcome to ensure balanced representation. The training set included 5355 participants, the validation set 1148 participants, and the testing set 1148 participants. Hyperparameters (learning rate, hidden units, dropout rate) were tuned using the validation set. Final performance was assessed in the testing set. Discrimination was evaluated using the area under the receiver operating characteristic curve - area under the curve (ROC AUC) and the area under the precision–recall curve – area under the curve (PR AUC). Additional performance metrics included sensitivity, specificity, precision, F1 score, and balanced accuracy, calculated at the probability threshold that maximized the Youden index.

Model interpretability

To enhance clinical interpretability, we quantified population-level feature importance to identify which periodontal features contributed most strongly to mortality prediction. Importance scores were derived across cross-validation folds, with higher values indicating greater influence on model predictions. This approach provided clinically meaningful insights into how probing depth, clinical loss of attachment, and missingness informed risk estimation.

Statistical analysis

All analyses were conducted using Python 3.10 (Python Software Foundation, Wilmington, DE, USA). Graph neural network models were implemented with the PyTorch Geometric library (PyTorch, Meta AI, Menlo Park, CA, USA). Model performance was evaluated in the independent test set using ROC and PR curves, with AUC values as the primary measures of discrimination. Secondary metrics included sensitivity, specificity, precision, F1 score, and balanced accuracy, calculated at the probability threshold maximizing the Youden index. Feature importance was quantified at the population level to identify the most influential predictors of mortality. NHANES survey weights were not applied, as the objective was individual-level risk prediction rather than estimation of population-level prevalence.

Results

Baseline characteristics of the study population, stratified by survival status, are presented in Table 1. A total of 9034 participants were included, of whom 1000 died during follow-up. Deceased participants were significantly older than survivors (69.7 ± 12.3 years vs. 52.1 ± 14.0 years, $P < 0.001$). In addition, males were more prevalent among the deceased group (53.5 %) than among survivors (47.5 %, $P < 0.001$). Racial and ethnic distributions differed between groups. The proportion of non-Hispanic white participants was higher in the deceased group ($P < 0.001$).

Table 1 Baseline characteristics of the study population stratified by mortality status.

Variable	Alive (N = 8034)	Deceased (N = 1000)	*P* value
Age (years)	52.14 ± 13.98	69.69 ± 12.32	<0.001
Male sex (%)	47.5	53.5	<0.001
BMI (kg/m^2)	29.33 ± 6.92	28.69 ± 7.24	0.01
Waist circumference (cm)	99.97 ± 15.84	102.28 ± 16.36	<0.001
Race/ethnicity (%)			
Mexican American	12.1	6.7	
Other Hispanic	9.9	5.9	
Non-Hispanic white	39	56.3	
Non-Hispanic black	22.9	24.4	
Other/multi-racial	16.1	6.7	<0.001
Education (%)			<0.001
< 9th grade	9.4	15.6	
9–11th grade	13.5	18.4	
High school/GED	21.5	25.3	
Some college/ AA	28.4	24.3	
College graduate+	27.2	16.4	
Smoking status (%)			0.004
Never	48.2 %	38.4 %	
Former	33.1 %	45.7 %	
Current	18.7 %	15.9 %	
Physical activity (%)			0.012
Active	42.6 %	31.4 %	
Insufficient	28.5 %	32.8 %	
Inactive	28.9 %	35.8 %	
Mean probing depth (mm)	1.58 ± 0.66	1.71 ± 0.68	<0.001
Mean loss of attachment (mm)	1.86 ± 1.06	2.46 ± 1.34	<0.001
Number of missing teeth	3.12 ± 4.28	7.85 ± 6.41	<0.001

N: number.
BMI: body mass index.
GED: general educational development.
AA: associate of arts degree.

Anthropometric measures showed statistically significant differences between the two groups. Mean body mass index (BMI) was lower among the deceased compared with survivors (28.7 ± 7.2 kg/m^2 vs. 29.3 ± 6.9 kg/m^2, $P = 0.01$), while waist circumference was higher (102.3 ± 16.4 cm vs. 100.0 ± 15.8 cm, $P < 0.001$), suggesting a greater central adiposity burden in the deceased group. Smoking status also differed significantly, with a higher prevalence of

current or former smokers among deceased group ($P < 0.001$).

Periodontal measures demonstrated marked disparities. Deceased participants had significantly greater mean probing depth (Alive = 1.58 ± 0.66 mm vs Deceased = 1.71 ± 0.68 mm, $P < 0.001$) and loss of attachment (Alive = 1.86 ± 1.06 mm vs Deceased = 2.46 ± 1.34 mm, $P < 0.001$) compared with survivors, indicating more severe periodontal destruction. The proportion of participants classified with moderate-to-severe periodontitis was substantially higher among those who died.

Fig. 2 summarizes the adjusted logistic regression models for all-cause and cardiovascular mortality. Both mean probing depth and mean loss of attachment exhibited strong, graded associations with mortality risk after adjustment for age and sex. Participants in higher quartiles of either measure had progressively higher adjusted probabilities of death for both outcomes (all P for trend <0.001). The adjusted all-cause mortality probability increased from 2.2 % to 5.6 % across quartiles of mean probing depth and from 2.2 % to 6.3 % across quartiles of mean loss of attachment. Similarly, the adjusted cardiovascular mortality probability increased from 0.38 % to 1.28 % across probing depth quartiles and from 0.58 % to 1.46 % across loss of attachment quartiles, indicating consistent dose—response gradients between greater periodontal destruction and elevated mortality risk.

Performance of the graph neural network for mortality prediction is summarized in Table 2 and illustrated in Fig. 3. For all-cause mortality, the model achieved a ROC AUC of 0.831 and a PR AUC of 0.397 (Fig. 3a and b). At the optimal threshold determined by the Youden Index (0.074), sensitivity was 0.833 and specificity was 0.694, with a precision of 0.253 and an F1 score of 0.388, yielding a balanced accuracy of 0.764.

For cardiovascular mortality, the ROC AUC was 0.845 and the PR AUC was 0.203 (Fig. 3c and d). At the optimal threshold (0.039), sensitivity was 0.812 and specificity was 0.758, with precision of 0.110 and an F1 score of 0.194, corresponding to a balanced accuracy of 0.785.

Although precision values were modest due to the low prevalence of events, the graph neural network consistently demonstrated strong discrimination and acceptable calibration across both outcomes. Feature importance analyses further confirmed probing depth and clinical loss of attachment as the strongest predictors, with missingness contributing additional prognostic information.

Population-level feature importance derived from the graph neural network is presented in Fig. 4a and b. For both all-cause and cardiovascular mortality, probing depth and clinical loss of attachment consistently emerged as the strongest predictors. The missingness indicator contributed less overall but still provided additional prognostic value. These findings underscore the robustness of probing depth and loss of attachment as primary drivers of mortality risk prediction.

Discussion

In this nationally representative study using NHANES 2011—2014 data, we applied a GCN to site-level periodontal

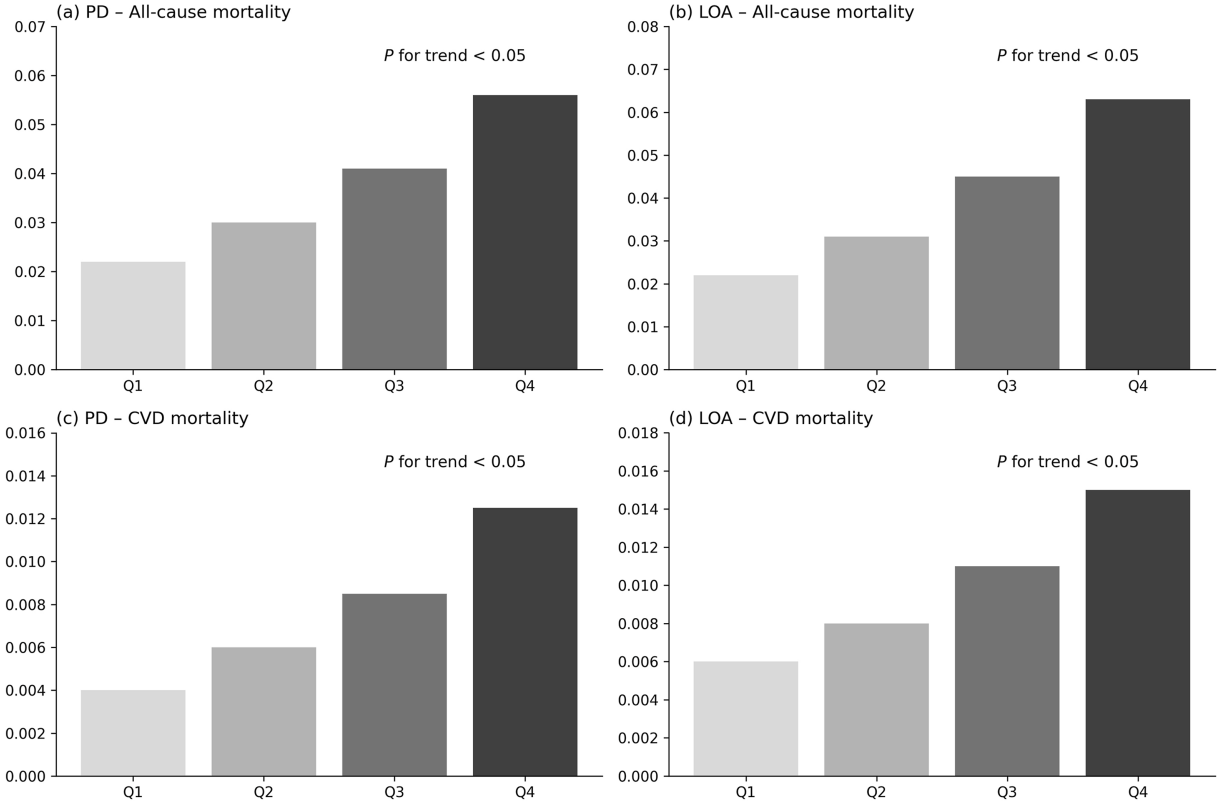

Figure 2 Adjusted mortality probability by quartiles of periodontal measurements.

Table 2 Performance metrics of individual models with optimal thresholds (Youden index).

Outcome	ROC AUC	PR AUC	Sensitivity	Specificity	Precision	F1 score	Balanced accuracy	Threshold
All-cause mortality	0.831	0.397	0.833	0.694	0.253	0.388	0.764	0.074
CVD mortality	0.845	0.203	0.812	0.758	0.11	0.194	0.785	0.039

ROC AUC: area under the receiver operating characteristic curve.
PR AUC: area under the precision–recall curve.
CVD: cardiovascular disease.

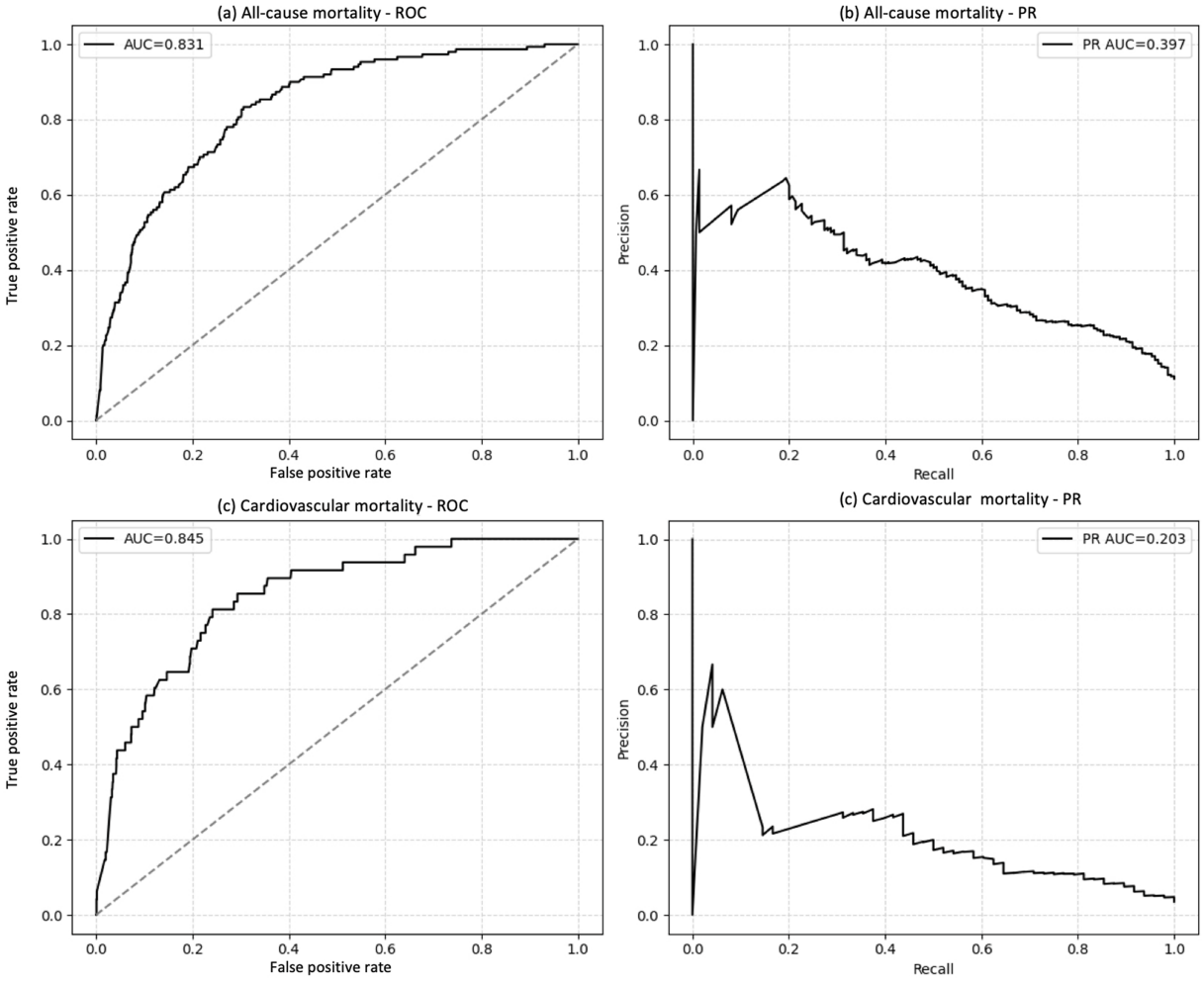

Figure 3 Receiver operating characteristic (ROC) and precision–recall (PR) curves of the graph neural network for predicting mortality. (a) ROC curve for all-cause mortality. (b) PR curve for all-cause mortality. (c) ROC curve for cardiovascular mortality. (d) PR curve for cardiovascular mortality.

measurements to predict all-cause and cardiovascular mortality. The model demonstrated strong discrimination, with ROC AUC values of 0.831 for all-cause mortality and 0.845 for cardiovascular mortality, although precision was modest, reflecting the relatively low number of events. Probing depth and clinical loss of attachment consistently emerged as the most influential predictors, while the missingness indicator contributed less overall but remained informative. These findings highlight the prognostic relevance of detailed periodontal measures and suggest that spatially structured graph-based models can provide meaningful insights into systemic health outcomes.

The relationship between periodontitis and mortality has been consistently observed in large epidemiologic studies, supporting its role as a systemic risk factor. NHANES-based analyses and *European* cohorts have reported increased risks of all-cause and cardiovascular mortality among individuals with poor periodontal health,[7,9,13] while prospective data such as the Sister Study confirmed associations between periodontal disease, tooth

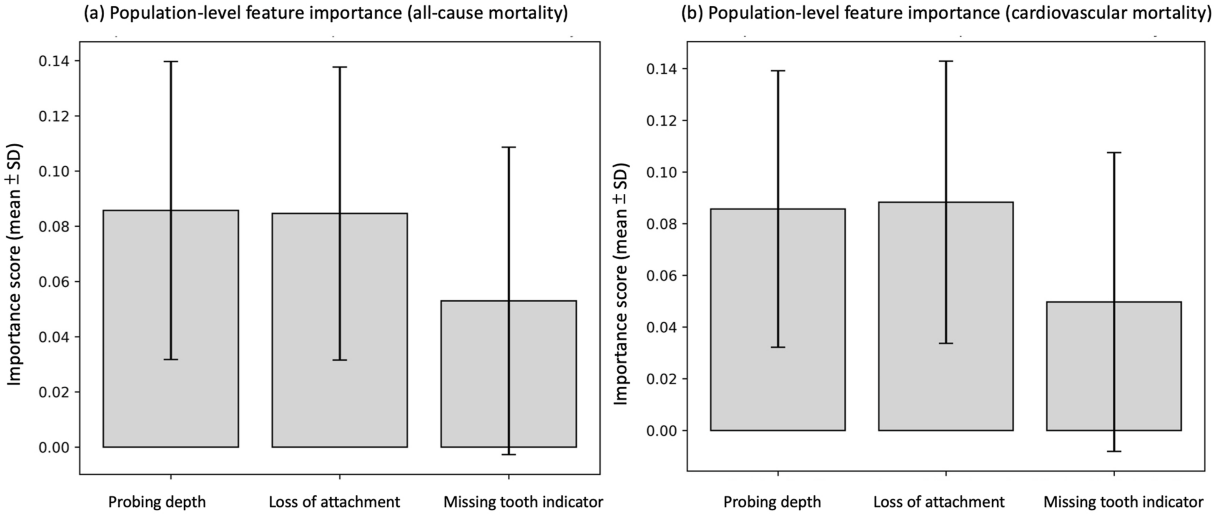

Figure 4 Population-level feature importance of graph neural network predictors. (a) All-cause mortality. (b) Cardiovascular mortality.

loss, and cause-specific mortality.[12] Severe attachment loss and deep probing depths have been shown to predict cardiovascular outcomes,[6,10] findings echoed in our analysis where both measures were the strongest contributors to risk. Studies in Asian populations have reinforced these associations, with Li et al.[11] demonstrating the prognostic significance of severe periodontitis in China. Collectively, this evidence highlights a consistent global pattern in which severe periodontitis elevates mortality risk.

Emerging research further underscores the interaction between periodontal disease and systemic conditions such as obesity, where shared inflammatory pathways contribute to worse outcomes.[17] Our findings that posterior sites with greater probing depth and attachment loss were highly influential align with this mechanistic framework, as localized severe lesions likely act as chronic inflammatory reservoirs. Surveillance data indicate that the prevalence of periodontitis remains high globally, with over 60 % of dentate adults affected and nearly one quarter experiencing severe disease.[1,2] In some regions, including Taiwan, prevalence has risen among younger adults,[18,] highlighting the urgency of early detection and intervention. Together, these perspectives converge with consensus reports recognizing periodontitis as a major contributor to systemic disease burden.[3]

Traditional studies often relied on categorical case definitions or aggregated indices, which can obscure spatial patterns of periodontal destruction.[9,12] Our GCN approach preserved site-level detail and anatomical adjacency, enabling detection of clinically meaningful patterns such as anterior—posterior interactions. Oss Boll et al.[15] noted that Graph Neural Networks are well suited for heterogeneous clinical data, as they integrate complex features and manage data sparsity. Similarly, Simon et al.[16] emphasized that non-Euclidean models better preserve structural relationships important for clinical prediction. The subgraph analyses in our study illustrate how these methods uncover nuanced inter-tooth relationships, advancing beyond traditional models and providing a more individualized risk assessment framework.

Interpretability analyses revealed that sites exhibiting higher probing depths and attachment loss, consistent with clinically defined moderate-to-severe periodontitis, were the strongest contributors to mortality prediction. This is biologically plausible given the complex root anatomy and plaque-retentive morphology of posterior teeth, which increase susceptibility to advanced periodontal destruction. Such localized lesions may elevate systemic inflammatory markers including C-reactive protein and interleukin-6,[4,5] known mediators of endothelial dysfunction and atherosclerosis.[3] Our findings also suggest that prognostic value is enhanced when multiple regions of the dentition are affected, underscoring the importance of considering spatial distribution in clinical assessments.

The strengths of this study include the comprehensive site-level periodontal measurements, linkage with long-term mortality follow-up, and the use of a graph-based deep learning model that preserved anatomical context. Nonetheless, limitations must be acknowledged. The observational design precludes causal inference, and residual confounding cannot be excluded. Precision for cardiovascular mortality was modest due to the relatively small number of events, a limitation shared with prior NHANES analyses.[9] NHANES survey weights were not applied, as our objective was prediction rather than estimation of population prevalence. Only baseline periodontal data were analyzed, limiting insights into disease progression. In addition, GCN models require considerable computational resources and technical expertise, which may limit immediate clinical implementation.[15] External validation remains necessary to confirm generalizability.

Finally, this study relied on baseline periodontal examinations, which may not fully capture the dynamic nature of periodontal disease progression. Longitudinal evidence has shown that the persistence and progression of periodontal inflammation are significant determinants of systemic disease and mortality risk.[4,5] For instance, studies with long-term follow-up have demonstrated that individuals with progressive attachment loss over time exhibit a higher risk of cardiovascular events compared to those with stable

periodontal conditions. While our GNN model effectively utilizes the spatial complexity of baseline data, future studies incorporating longitudinal measurements would provide deeper insights into the temporal mechanisms linking periodontal health to mortality.

Future research should focus on external validation in independent and non-U.S. cohorts, integration with systemic biomarkers and imaging data, and incorporation of longitudinal periodontal measures to capture disease progression. Simon et al.[16] highlighted the potential of multimodal and non-Euclidean approaches to further strengthen clinical translation. Development of accessible decision support systems that incorporate GNN-based outputs may bridge dental and medical care, enabling earlier identification of high-risk individuals and guiding preventive interventions.

In summary, a graph convolutional network applied to site-level periodontal data from NHANES 2011—2014 demonstrated strong discrimination for predicting both all-cause and cardiovascular mortality, with ROC AUC values of 0.831 and 0.845, respectively. By incorporating probing depth, clinical loss of attachment, and a missingness indicator while preserving anatomical relationships, the model provided clinically meaningful prognostic information beyond traditional case definitions. These findings reinforce the importance of periodontal health in systemic risk assessment and highlight the potential of graph-based deep learning to improve precision in mortality risk prediction.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

This study did not receive any external funding resources.

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