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Use of serum albumin levels and salivary biomarkers in assessing periodontal disease: a community hospital perspective

Ping-Chen Chung[1] and Ta-Chien Chan[2,3,4,5*]

Abstract

Background Periodontal status can be reflected in serum and oral biomarkers. Salivary biomarkers are novel screening tools for individuals with dentophobia or disabilities. This study aimed to explore the differences in SiLL-Ha results and serum albumin levels between clinical attachment loss (CAL) ≥ 5 mm (Group A) and CAL < 5 mm (Group B) as well as the influence of sex on these differences.

Methods This study recruited healthy adults aged 35–80 years from a community hospital. Participants completed a demographic questionnaire. We collected the participants' medical history, including hypertension, diabetes mellitus (DM) and hyperlipidemia, from electronically stored medical records. Additionally, they underwent a collaborated saliva test, an oral examination including records of clinical attachment levels, and a blood test to measure albumin levels sequentially. Participants were divided into Group A and Group B based on a CAL cut-off point of 5 mm. Multivariable logistic regression was used to analyze associations between the SiLL-Ha results, serum albumin levels, periodontitis, and sex stratification.

Results The mean age of the 231 participants was 64.4 years, and 58.4% were women. Older age, low serum albumin levels, and high blood levels of SiLL-Ha were associated with periodontitis. Among the women, age and blood level of SiLL-Ha output were significantly associated with periodontitis. Among men, serum albumin level was significantly associated with periodontitis. Participants with DM were less likely to have periodontitis, particularly females.

Conclusions The saliva test is a noninvasive tool applicable not only in dental clinics but also in community settings. It is beneficial for self-monitoring of oral health and promoting health awareness and behavior.

Keywords SiLL-Ha, Salivary test, Periodontitis, Community hospital

Background

Individuals with dentophobia may avoid dental treatment even when experiencing severe oral pain. A recent meta-analysis estimated the global prevalence of dental fear and anxiety at 15.3% (95% confidence interval [CI]: 10.2, 21.2), with a higher prevalence among women (19.1%) [1]. In Taiwan, the estimated prevalence of dental anxiety was estimated to be 20.6% among 5–8 year-old children [2]. In dental practice, current management strategies for relieving and mitigating dental fear include virtual reality distraction techniques, music therapy, aromatherapy, and cognitive-behavioral therapy [3]. For individuals,

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especially those with dentophobia, serum and salivary biomarkers serve as useful screening tools for target oral diseases, including periodontitis [4, 5]. Traditionally, the stage of periodontitis is diagnosed by assessing clinical attachment loss (CAL) [6]. Serum biomarkers, including C-reactive protein, matrix metalloproteinases [4], interleukins [7], and tumor necrosis factor-alpha [8] are useful for diagnosing and monitoring periodontitis in both treated and untreated patients and for evaluating treatment response. Moreover, serum albumin is a marker of periodontitis, which is associated with inflammation and infection [9]. Inflammation decreases serum albumin levels [10].

Various saliva tests have been developed [4]. SiLL-Ha (https://sillhasaliva.com/), is portable saliva test system using optical detection to assess the risk of periodontal disease and caries, as well as to evaluate oral cleanliness. The SiLL-Ha system is suitable for routine screening and rapid reporting. Users can follow the suggestions provided by the SiLL-Ha results to improve their oral hygiene and seek professional dental advice and treatments. To date, few studies have applied the SiLL-Ha in oral health screening programs. A previous study reported that leukocyte esterase activity, as measured using SiLL-Ha, significantly differed between the baseline and final examinations (9 months after the baseline examination). All 36 participants underwent scaling and root planing, followed by a re-examination 3 months after the baseline. Subsequently, participants received supportive periodontal therapy every 3 months, with the final examination conducted 6 months after the re-examination [11]. In another study, 34 individuals with a >5 mm pocket depth had higher leukocyte and protein levels, as measured by SiLL-Ha, than 70 individuals with a pocket depth of ≤ 5 mm [12].

This study aimed to identify individuals with high risk of periodontitis (CAL ≥ 5 mm) in a community hospital setting and to explore the differences in SiLL-Ha results and serum albumin levels between these individuals and those with CAL < 5 mm. The secondary objective was to examine whether these differences were influenced by sex.

Methods

Study participants

This study was conducted at the Dental Department of Puzi Hospital, Chiayi County, Taiwan between November 01, 2021, and December 31, 2022. Participants were healthy adults aged 35–80 years. Exclusion criteria included a history of pharyngeal and laryngeal surgery, stroke, cerebral palsy, myasthenia gravis, oral cancer, aspiration pneumonia, moderate-to-severe Parkinson's disease, moderate-to-severe dementia, or Alzheimer's disease. Written informed consent was obtained from all participants after they fully understood the study. This study was approved by the Institutional Review Board of Biomedical Science Research, Academia Sinica (AS-IRB-BM-21047).

The sample size was determined by rejecting the null hypothesis using a two-tailed test with an effect size of 0.5, a significance level of 0.05, and a power of 0.95. The suggested sample size was 220 participants. In total, 231 participants were recruited.

Participants were divided into Group A and Group B. The Group A was defined based on the criteria established by the American Academy of Periodontology (AAP) and European Federation of Periodontology (EFP) [13]. Those with at least one site exhibiting a CAL of ≥ 5 mm were classified in the Group A [6].

Data collection

Participants completed a demographic questionnaire (Supplement). Participants completed a demographic questionnaire (Supplement). We collected the participants' medical history, including hypertension, diabetes mellitus (DM), and hyperlipidemia, from electronically stored medical records. Additionally, they underwent a collaborative saliva test, an oral examination including records of clinical attachment levels, and a blood test to measure albumin levels sequentially. Saliva testing was performed using SiLL–Ha (SILL–Ha® ST–4910; ARKRAY Inc., Kyoto, Japan) by following the manufacturers' instructions (https://www.arkrayusa.com/sites/arkrayusa.com/files/SiLL–Ha_Operating_Manual.pdf). The participants were instructed not to drink, eat, or brush their teeth for 2 h before testing. Participants were asked to spit their saliva sample into a paper cup after rinsing of mouth with 3 mL of sterile water for 10 s. A droplet of the sample was placed on a test strip and loaded into the instrument for measurement. The analyzer measured cariogenic bacteria, acidity, buffer capacity, blood, leukocyte, protein, and ammonia. The value of each test item ranged from 0 to 100.

Participants underwent blood testing for albumin measurement. Serum albumin levels were analyzed using the Automatic Clinical Chemistry Analyzer TBA-NX360 (Canon, Japan), employing the bromocresol green method with the BioAccut ALB Kit (TUNYEN, Taiwan).

Statistics analysis

The chi-square test was performed to compare the distribution of sex, hypertension, DM and hyperlipidemia between the Group A and Group B. Fisher's exact tests were used to determine the association between smoking and periodontal status. The Mann–Whitney U test was used to compare the differences in age, saliva test results,

and serum albumin levels between the Group A and Group B for non-normally distributed data, after conducting the Shapiro–Wilk normality test. The distribution of periodontal parameters, including the mean CAL and number of sites with deep CAL of 5 mm or more, was calculated. We conducted the Spearman correlation test to explore the correlation between the number of sites with deep CAL of 5 mm or more and biochemical parameters, including serum albumin levels and SiLL-Ha results. Multivariable logistic regression models were used to analyze the associations between the SiLL-Ha results, serum albumin levels, periodontal status, and stratification by sex. Since all female participants were non-smokers, smoking habits were not included in the logistic regression with sex stratification. The area under the receiver operating characteristic curve (AUC) and receiver operating characteristic (ROC) curve were used to evaluate the predictive performance of salivary and serum biomarkers. Additionally, a combined approach using logistic regression was applied after adjusting for age, sex, and medical history of hypertension, DM, and hyperlipidemia. Statistical significance was set at $p < 0.05$. The R software (version 4.3.1) [14] was used for all data management and statistical analyses.

Results

This study included 231 participants with a mean age of 64.4 years (standard error [SE] = 0.74), of whom 135 participants were female, accounting for 58.4%. Participants with hypertension, DM, and hyperlipidemia accounted for 14.3%, 25.5%, and 32.9%, respectively. Nonsmokers accounted for 88.3% of the total population. SiLL-Ha outputs yielded the following results: mean score of cariogenic bacteria, 16.9 (SE = 1.32); acidity, 64.8 (SE = 1.50); buffer capacity, 11.2 (SE = 0.88); ammonia, 21.2 (SE = 1.24); blood, 36.4 (SE = 1.71); leukocytes, 58.6 (SE = 2.03), and protein, 32.4 (SE = 1.26). The mean serum albumin level was 4.2 g/dL (SE = 0.01). The normal range for adults younger than 60 years is 3.5–5.2 g/dL and for adults aged 60 years and older is 3.2–4.6 g/dL (Table 1).

Table 1 Differences in salivary screening results according to the clinical attachment level

	Total (*n* = 231)	**Group B CAL < 5 mm (*n* = 103)**	**Group A CAL ≥ 5 mm (*n* = 128)**	***P* value**
Age	64.4 (0.74)	61.1 (1.28)	67.2 (0.77)	< 0.001
Sex				0.69
Female	135 (58.4%)	62 (60.2%)	73 (57.0%)	
Male	96 (41.6%)	41 (39.8%)	55 (43.0%)	
Hypertension				0.85
No	198 (85.7%)	89 (86.4%)	109 (85.2%)	
Yes	33 (14.3%)	14 (13.6%)	19 (14.8%)	
DM				0.049
No	172 (74.5%)	70 (68.0%)	102 (79.7%)	
Yes	59 (25.5%)	33 (32.0%)	26 (20.3%)	
Hyperlipidemia				0.67
No	155 (67.1%)	71 (68.9%)	84 (65.6%)	
Yes	76 (32.9%)	32 (31.1%)	44 (34.4%)	
Smoking				0.6
No	204 (88.3%)	90 (87.4%)	114 (89.1%)	
Yes	10 (4.3%)	6 (5.8%)	4 (3.1%)	
Ever, but quit	17 (7.4%)	7 (6.8%)	10 (7.8%)	
Cariogenic bacteria: n (SE)	16.9 (1.32)	16.5 (1.75)	17.3 (1.93)	0.84
Acidity: n (SE)	64.8 (1.50)	65.0 (2.28)	64.7 (1.99)	0.79
Buffer capacity: n (SE)	11.2 (0.88)	11.2 (1.20)	11.2 (1.26)	0.97
Ammonia: n (SE)	21.2 (1.24)	18.9 (1.60)	23.1 (1.81)	0.15
Blood: n (SE)	36.4 (1.71)	32.7 (2.50)	39.5 (2.32)	0.04
Leukocyte: n (SE)	58.6 (2.03)	56.4 (3.04)	60.3 (2.73)	0.25
Protein: n (SE)	32.4 (1.26)	31.1 (1.88)	33.5 (1.71)	0.28
Albumin: n (SE)	4.2 (0.01)	4.29 (0.02)	4.19 (0.02)	< 0.001

Abbreviation: CAL Clinical attachment level, *SE* Standard error

The mean CAL was 1.94 (SE = 2.08) and number of sites with deep CAL of 5 mm or more was 5.17 (SE = 0.54).

In total, 128 participants were classified as Group A and 103 participants were classified as the Group B. Age, DM, blood level of SiLL-Ha, and serum albumin levels were significantly different between the Group A and Group B. In the Group A, the mean age was higher (mean = 67.2, SE = 0.77), blood levels of SiLL-Ha were higher (mean = 39.5, SE = 2.32), and serum albumin levels were lower (mean = 4.19, SE = 0.02) than those in the Group B (Table 1). However, a higher percentage of participants in the Group B (32.0%) than in the Group A (20.3%) had DM. Serum albumin, as well as blood and ammonia levels from the SiLL-Ha results, were significantly correlated with CAL. Participants with older age, low serum albumin, and high blood levels of SiLL-Ha were more likely to develop periodontitis. Among women, older adults (coefficient = 0.07; 95% CI: 0.03, 0.12) and participants with high blood level of SiLL-Ha output (coefficient = 0.03; 95% CI: 0.01, 0.05) had higher risk to have periodontitis. Among men, low serum albumin level (coefficient = -5.02; 95% CI: -8.25, -2.21) were associated with a higher probability of periodontitis (Table 2). Participants with DM were less likely to have periodontitis, particularly females.

The AUC values, which indicate predictive performance, for salivary biomarkers, serum biomarkers, and the combined approach were 0.72, 0.70, and 0.73, respectively. The ROC curves, for salivary biomarkers, serum biomarkers, and the combined approach were presented in Fig. 1A, B, and C.

Discussion

Older age, no DM diagnosis, high blood SiLL-Ha levels, and lower albumin levels were associated with periodontitis. Sex differences were observed in the relationship between serum albumin, blood levels of SiLL-Ha, and periodontitis. Aging is a time-dependent impairment of biomechanisms, including changes in the immune response [15]. Aging induces dysregulation of the immune response, which increases the susceptibility to inflammatory response [16]. Middle-aged and older adults have a high prevalence of periodontal disease and gingival bleeding, and deep periodontal pockets [17].

Free hemoglobin levels differ significantly between individuals with severe periodontitis and those without periodontal disease [18]. Free hemoglobin concentration was higher in the severe periodontitis group than in the no periodontal disease group. Severe periodontitis was classified as having at least one probing depth of 6 mm or more [18]. Moreover, a deeper periodontal pocket depth is associated with a significantly higher incidence of bleeding on probing, indicating inflammation of the periodontal tissue [19]. Bleeding is a sentinel sign of periodontitis risk. Self-reported gingival bleeding during brushing [20] and self-reported bleeding gums [21] help predict periodontitis and distinguish periodontal health and disease.

In this study, women in the Group A had significantly higher blood levels from SiLL-Ha scores than women in the Group B. Changes in hormone levels due to menopause may contribute to this finding [22]. Estrogen deficiency negatively affects the immune response. In the postmenopausal stage, levels of pro-inflammatory cytokines increase and immune responses to pathogens decrease, causing high susceptibility to infection [22]. Cytokines such as interleukin (IL)-6 promote active bone resorption and periodontal inflammation [22, 23].

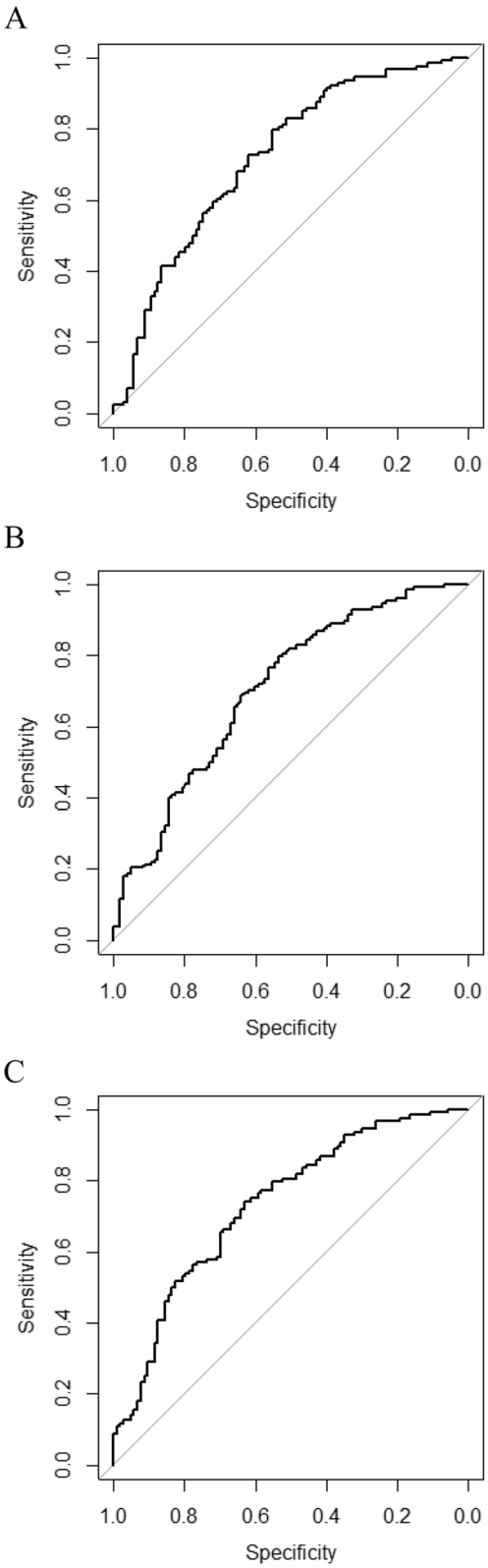
An inverse relationship exists between serum albumin levels and the severity of chronic periodontitis [24]. Decreased serum albumin levels have also been reported in patients with aggressive periodontitis [25]. In one study, the chronic periodontitis group showed a decline in serum albumin levels after 3 months of non-surgical periodontal treatment compared with the healthy periodontal group [24]. Microorganisms cause destruction of the periodontal tissue and lead to change of inflammatory cytokines concentration such as IL-1β, IL-6, and tumor necrosis factor-alpha [24]. However, serum albumin concentration is also influenced by nutritional status, especially in older adults with impaired dentition and systemic diseases. Albumin is a useful index of periodontal inflammation, but the explanation should be concluded carefully [26]. There was no clear explanation for the significant association between serum albumin levels and periodontitis observed only in men. Sex disparities in biology, microbial etiology, socioeconomic status, lifestyle, and behavior may play a role in periodontal disease [27].

DM exacerbates susceptibility to periodontitis by impairing the immune response, inducing both local and systemic inflammatory responses, decreasing collagen turnover, and altering the subgingival microbial profile [28, 29]. In our study, participants were recruited from a single hospital. The proportion of participants with DM was lower in the Group A than in the Group B, which is different from the results of nationwide, large population-based retrospective cohort studies [30–32]. Studies using the Taiwan National Health Insurance Research Database show a higher prevalence of DM among patients with periodontitis than among those without periodontitis. Contrary to previous study findings, our results showed that individuals without a DM diagnosis had a higher risk of periodontitis [28, 29], which may be attributed to the small sample size of our study.

Table 2 Relationship between periodontitis and salivary screening results, stratified by sex

	Total		Female		Male	
	Coefficient 95% CI	***P* value**	**Coefficient 95% CI**	***P* value**	**Coefficient 95% CI**	***P* value**
Age	0.05(0.02,0.09)	0.002**	0.07(0.03, 0.12)	0.003**	0.01(-0.04, 0.06)	0.72
Sex						
Female	Ref					
Male	0.26(-0.42, 0.94)	0.46				
Smoking						
No	Ref					
Yes	0.30(-1.28, 1.84)	0.70				
Ever, but quit	0.46(-0.78, 1.74)	0.47				
Hypertension						
No	Ref					
Yes	-0.27(-1.13, 0.60)	0.54	-0.17(-1.46, 1.16)	0.79	-0.10(-1.36, 1.21)	0.88
DM						
No	Ref					
Yes	-1.11(-1.84, -0.40)	0.003**	-1.14(-2.17, -0.17)	0.02*	-0.80(-1.97, 0.32)	0.16
Hyperlipidemia						
No	Ref					
Yes	0.44(-0.22, 1.12)	0.20	0.21(-0.66, 1.09)	0.64	0.74(-0.39, 1.96)	0.21
Albumin	-1.95(-3.67, -0.29)	0.02*	-0.13(-2.43, 2.20)	0.91	-5.02(-8.25, -2.21)	0.001 **
Cariogenic bacteria	0.005(-0.01, 0.02)	0.55	0.003(-0.02, 0.03)	0.82	0.01(-0.02, 0.03)	0.63
Acidity	-0.01(-0.03, 0.01)	0.24	-0.01(-0.03, 0.02)	0.53	-0.01(-0.03, 0.02)	0.63
Buffer capacity	-0.02(-0.05, 0.01)	0.20	-0.03(-0.07, 0.02)	0.24	-0.001(-0.05, 0.05)	0.95
Ammonia	0.01(-0.01, 0.03)	0.27	0.02(-0.01, 0.04)	0.21	-0.005(-0.04, 0.03)	0.78
Blood	0.02(0.001, 0.03)	0.04*	0.03(0.01, 0.05)	0.02*	-0.003(-0.03, 0.02)	0.79
Leukocyte	0.001(-0.01, 0.01)	0.84	0.001(-0.02, 0.02)	0.95	-0.002(-0.02, 0.02)	0.83
Protein	-0.01(-0.03, 0.01)	0.48	-0.01(-0.05, 0.02)	0.49	0.002(-0.03, 0.04)	0.92

Abbreviation: *CI* confidence interval; *:*P* value < 0.05, **:*P* value < 0.01



◀ **Fig. 1** The ROC curves for salivary biomarkers, serum biomarkers, and the combined approach. **A** The ROC curves for salivary biomarkers. **B** The ROC curves for serum biomarkers. **C** The ROC curves for the combined approach

SiLL-Ha, a monitoring tool for oral health risk assessment, uses a relatively quick and easy method to collect saliva. The multiparameter salivary test was performed using wavelength reflectance measurements in a short time. This test allows users to routinely self-monitor their oral health and aids in identifying oral conditions, such as dental caries, periodontal disease, and oral malodor. A study involving 36 participants using SiLL-Ha showed a significant difference in leukocyte esterase activity between the baseline and final examinations (9 months after baseline), however, no significant differences were observed in protein and ammonia levels. During the period between the baseline and final examinations, participants received one periodontal treatment and two supportive periodontal therapies [11]. A cross-sectional study involving 104 participants using Sill-Ha reported a significant difference in protein and leukocyte levels between groups with probing depths ≥ 5 mm and < 5 mm [12]. Higher protein and leukocyte levels were associated with deeper probing depths. Additionally, blood levels were elevated in the ≥ 5 mm group compared to the < 5 mm group ($P = 0.058$). In our study, we combined saliva and serum biomarkers to screen for potential periodontal disorders, investigate sex differences in biomarker levels, and assess oral health awareness. Our findings indicated that both Sill-Ha blood values and serum albumin levels were significantly associated with periodontal status. Specifically, Sill-Ha blood values showed a stronger association with periodontal status among females, while serum albumin levels were more strongly associated among males. The AUC of study from Deng et al. proposed active matrix metalloproteinase-8 for discriminating periodontal health was superior to that in our study (AUC = 0.883) [33]. The subgingival microbial dysbiosis index, computed at the species and genus levels, was used for the integrated data analysis. The results showed the accuracy of periodontitis diagnosis based on the subgingival microbial dysbiosis index for subgingival biofilm, saliva, and tongue had AUC values ranging 0.76–0.90 [34].

This study had several limitations. First, this was a cross-sectional study based on a community dataset; therefore, it did not provide evidence of a temporal relationship and causal inference was not possible. Potential selection bias may limit the extrapolation of our findings to the whole population. Therefore, future studies should recruit participants from diverse

community settings and include a longitudinal follow-up of participants. Moreover, potential confounding factors—such as health behaviors, routine dental examinations, gingival health indicators (e.g., bleeding on probing and probing depth), oral hygiene maintenance, recent periodontal treatment (within the past six months), antibiotic use within the last three months, and pregnancy or lactation status—should be considered in future studies. The incorporation of more comprehensive data enhanced the predictive performance of the model.

Conclusion

The saliva test is a noninvasive and rapid screening tool that can monitor oral status in a timely manner and has the advantage of easy sample collection. Its applicability extends to community settings, making it particularly beneficial for regular self-monitoring of people with disabilities, difficulty moving, and dentophobia. By providing accessible insights into oral status, the test empowers individuals to monitor their oral health regularly and seek timely dental care based on the results.

Abbreviations

CI	Confidence interval
CAL	Clinical attachment loss
DM	Diabetes mellitus
AUC	Area under the receiver operating characteristic curve
SE	Standard error
IL	Interleukin
ROC	Receiver operating characteristic curve

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12903-025-06042-x.

Supplementary Material 1.

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Authors' contributions

PCC contributed to conception, design, data collection, data analysis, interpretation and drafted the manuscript. TCC contributed to conception, design, and interpretation, acquired to research resources, and critically revised the manuscript. All the authors have read and approved the final manuscript.

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Data availability

The datasets generated and analyzed during the current study are not publicly available due to the informed consent, which specifies that any secondary use must be reviewed and approved by the Institutional Review Board (IRB) of Academia Sinica. However, the data are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Review Board (of Biomedical Science Research, Academia Sinica (AS-IRB-BM-21047). Written informed consent was obtained from all participants. This study was performed in accordance with the Declaration of Helsinki and followed the approved protocol.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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