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RESEARCH

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The role of childhood overweight in meibomian gland dysfunction and dry eye disease in Chinese children

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Abstract

Aim To explore the factors causing structural abnormalities of meibomian gland in the pediatric population.

Methods Two-hundred children were enrolled to evaluate the morphology of meibomian gland. Demographic and clinical information were collected. Symptoms of dry eye disease (DED) were assessed with the ocular surface disease index (OSDI) questionnaire. Meibography was performed and grading of images was performed by a 5-point meiboscale (0–4) for gland atrophy and a 3-point score (0–2) for gland tortuosity.

Results 200 eyes of 200 participants aged 10–18 years (13.10 ± 2.39 years) were imaged. Most patients had a score of 1, 130 (65%) in meiboscore and 138 (69%) in gland tortuosity. The meiboscore showed significant difference with the increase of weight, BUT and BMI percentile ranking. The gland tortuosity showed significant difference with the increase of age, and BMI percentile ranking. Besides, shorter BUT corresponds to larger percentage of meibomian gland atrophy and higher OSDI score. Gender had no significant effect on gland dysfunction. The gland meiboscore was significantly correlated with weight, OSDI score, BUT, BMI percentile and BMI percentile ranking. And the gland tortuosity was significantly correlated with weight, BMI percentile and OSDI score.

Conclusion In this pediatric population, the meiboscore become higher with the increase of weight, BMI percentile, OSDI and the decrease of BUT, and gland tortuosity became more serious with the increase of age and BMI percentile. Therefore, clinicians should be aware that being overweight is a risk factor for changes in meibomian gland structure.

Keywords Meiboscale, Gland tortuosity, Body mass index percentile, Children

Introduction

Meibomian gland dysfunction (MGD) is a chronic and diffuse condition affecting the meibomian glands, primarily characterized by terminal duct obstruction and alterations in the quality or quantity of palpebral lipid secretion. Clinically, it can lead to an abnormal tear film, eye irritation symptoms, ocular surface inflammation, increased tear evaporation, and tear film instability, all of which ultimately contribute to the development of dry eye disease (DED) [1]. The prevalence of MGD reported in published studies varies substantially, ranging from 3.5% to nearly 70%. A notable observation when

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reviewing these publications is that the prevalence of MGD seems to be higher in studies conducted within Asian populations [1, 2]. Several risk factors for MGD have been identified, including dyslipidemia, advanced age, low-humidity environments, androgen depletion, systemic medications, and the use of orthokeratology lenses [3, 4, 5, 6]. With the increasing popularization of electronic products, the incidence rates of meibomian gland dysfunction (MGD) and dry eye disease (DED) are rising, and the age distribution is exhibiting a trend toward younger populations [7, 8].

Previous research conducted on American adolescents has shown that the extent of meibomian gland distortion correlates with body mass index (BMI) percentile. More specifically, an increase in BMI percentile is associated with a tendency for the tear film lipid layer thickness to decrease [9]. In view of the rapid changes in the dietary habits and lifestyles of Chinese residents, the problem of childhood obesity has become increasingly prominent [10]. The prevalence of overweight among Chinese children aged 6–12 years showed an increasing trend from 1993 to 2009 [11]. Owing to variations in gender and ethnicity, the distribution of BMI among Chinese children differs from that observed in other countries [12]. Previous report revealed changes in meibomian gland morphology and function in adolescents [13], and timely therapeutic meibomian gland massage has been demonstrated to have a positive impact on the meibomian glands [14]. Therefore, it is imperative to investigate the correlation between meibomian gland structure and childhood overweight in China in order to facilitate timely intervention. In this study, the morphology of meibomian glands was examined in a large cohort of children using a non-invasive ocular surface analyzer. The analysis focused on determining whether meibomian gland atrophy and tortuosity in children are associated with factors such as age, gender, BMI percentile, and other ocular surface parameters.

Methods

This study enrolled children who visited Yongkang Hospital between January 1, 2023 and August 31, 2023. The patients' medical histories were reviewed, and relevant information was collected, including age, gender, height, weight, ocular history, history of ocular surgery, previous or ongoing medication use, and findings from anterior segment biomicroscopy. Inclusion criteria included ages less than18 years and ability to cooperate with acquisition of meibomian gland images. Exclusion criteria comprised a prior diagnosis of meibomian gland dysfunction (MGD), dry eye disease (DED), allergic conditions, Sjögren's syndrome, or any other systemic disorders impacting meibomian gland function. Additionally, individuals with telangiectasia along the eyelid margin, eyelid defects, or ectopic meibomian gland orifices were also excluded.

The patient's body mass index (BMI) was calculated and recorded. And we calculated age- and sex-specific BMI percentiles using the "http://pro.healthykids.nsw.gov.au/assess/"(Assess - Healthy Kids for Professionals) website. Data on the website sourced from the Centers for Disease Control and Prevention (CDC) (2000). BMI for age chart takes the age, height, weight and sex of the child into consideration. The CDC charts are appropriate for children aged 2 to 18 years old. All children were required to complete the ocular surface disease index (OSDI), an internationally accepted assessment scale for the detection of subjective dry eye symptoms on a scale of 0 to 100. OSDI scores ≤ 20 was classified as mild symptoms, 21–45 as moderate symptoms, and ≥ 46 as severe symptoms.

The Keratograph 5 M Ocular surface analyzer (Oculus, Germany, model 77000) was used to observe and analyze the morphology of the meibomian glands and the opening of the meibomian glands, and to image the upper and lower meibomian glands of patients (Fig. 1). At the same time, non-invasive tear break-up time (BUT) and tear meniscus height (TMH) were also measured. Image grading was performed by experienced ophthalmologists using a proven 5-point scale of meibomian gland atrophy [15, 16]: grade 0: normal meibomian glands, grade 1: ≤25% gland atrophy, grade 2: 26–50% gland atrophy, grade 3: 51–75% gland atrophy, and grade 4:>75% gland atrophy. Meibomian gland tortuosity was scored on a 3-point scale [17]: distortion/tortuosity was defined as a > 45° angle of the meibomian gland, grade 0: no distortion, grade 1: 1 to 4 glands distorted, and grade 2: 5 or more glands distorted.

The data analysis for this paper was generated using SPSS software (version 26.0; SPSS, Inc., Chicago, IL, USA). Measurement data conforming to normal distribution were represented by mean ± SD, independent Samples t-test was used for comparison between the two groups, and one-way analysis of variance (ANOVA) was used for comparison among the three groups. To further elucidate the relationship between BMI and structural abnormalities of meibomian glands, we compared the age- and sex-specific BMI percentile ranking (0–20, 20–40, 40–60, 60–80,80–100) between groups. Differences of gender, meiboscore, gland tortuosity and BMI grade among the groups were determined by the x^2 test. Spearman correlation analysis was used to analyze the correlation among categorical variables and continuous variables. $P < 0.05$ were considered statistically significant.

The study was performed in accordance with the tenets of the Declaration of Helsinki and the Institutional

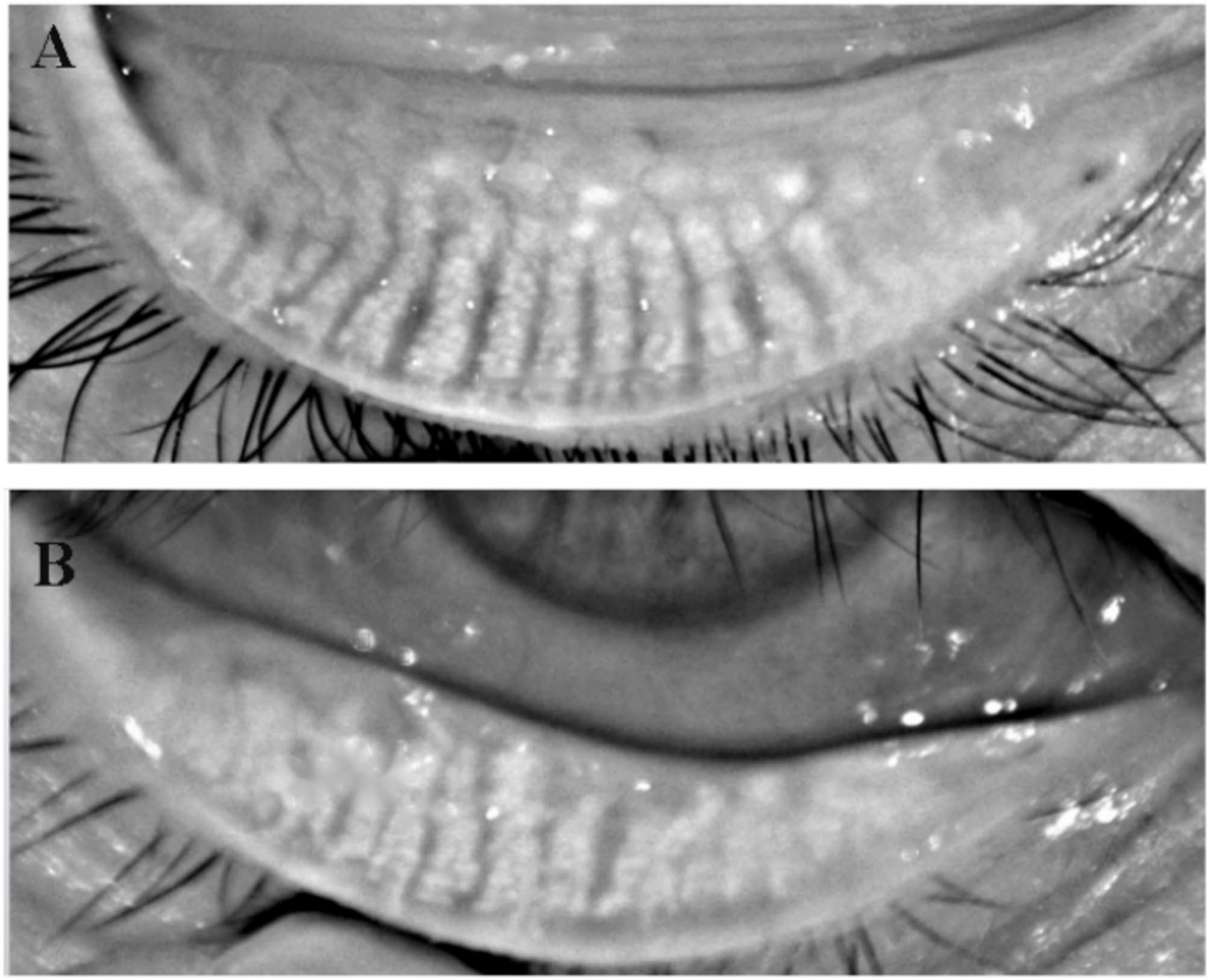

Fig. 1 Meibography of two patients' right lower eyelids: (**A**) 17-year-old child with normal BMI (21.5) that has preserved meibomian gland architecture (meiboscore 0, gland tortuosity 0). (**B**) 17-year-old obese child (BMI: 33.7) show meibomian gland atrophy and tortuosity (meiboscore 2, gland tortuosity 1)

Table 1 Basic characteristics of the subjects

Variable	N = 200	Variable	N = 200
Age (years)	13.10 ± 2.39	Meiboscore	
Weight (kg)	45.77 ± 14.37	0	45(22.5)
Height (cm)	151.52 ± 13.71	1	130(65)
BMI	19.56 ± 4.13	2	21(10.5)
OSDI	18.16 ± 13.33	3	4(2)
BUT (s)	8.67 ± 4.72	4	0(0)
TMH (mm)	0.15 ± 0.09	BMI percentiles	
Gender		1	68(34)
Male	92(46)	2	18(9)
Female	108(54)	3	38(19)
Tortuosity		4	33(16.5)
0	33(16.5)	5	48(24)
1	138(69)		
2	29(14.5)		

BMI, body mass index; OSDI, ocular surface disease index; BUT, tear break-up time; TMH, tear meniscus height

Review Board/Ethics Committee of Yongkang Hospital approved the study protocol.

Results

A total of 200 eyes of 200 participants were imaged. Mean age of the subjects was 13.10 ± 2.39 years (range 10–18 years). One hundred and eight participants (54%) were female, and 92 participants (46%) were male. All demographic information was summarized in Table 1. Mean weight and height of the subjects was 45.77 ± 14.37 kg and 151.52 ± 13.71 cm. The average BMI of the children in this study was 19.56 ± 4.13 kg/m^2. Previous studies have suggested that the BMI of normal weight in Chinese population ranges from 18.5 to 23.9 kg/m^2 [18, 19], and the BMI of obese patients is greater than 28 kg/m^2 [9]. The majority of the subjects (86%) have BMIs within the normal range.

Table 2 Differences between the gender

	Male	Female	*P*
N	92	108	
Age (years)	13.13	13.07	0.004
OSDI	18.58	17.80	0.226
BUT(s)	8.02	9.22	0.393
TMH (mm)	0.15	0.16	0.190
BMI percentile	52.68	48.55	0.297
Meiboscore			
0	21	24	0.636
1	58	72	
2	10	11	
3	3	1	
Tortuosity			
0	15	18	0.965
1	63	75	
2	14	15	
BMI percentile ranking			
1	29	34	0.323
2	5	13	
3	16	22	
4	15	18	
5	27	21	

BMI, body mass index; OSDI, ocular surface disease index; BUT, tear break-up time; TMH, tear meniscus height

In this study, the patients had a meiboscore of 0, 1, 2, 3 and 4 were 54 (22.5%), 130 (65%), 21 (10.5%), 4(2%) and 0 (0%) respectively. And the patients had a gland tortuosity score of 0, 1, and 2 were 33 (16.5%), 138 (69%) and 29 (14.5%) respectively. The mean OSDI questionnaire score was 18.16 ± 13.33. Mean BUT and TMH of the subjects was 8.67 ± 4.72s and 0.15 ± 0.09 mm.

Gender had no significant effect on meiboscore and gland tortuosity

There was no significant difference between male and female for all indexes except for age as seen in Table 2.

BMI percentile has significant influence on the majority parameters of ocular surface

As the BMI percentile increases, both the BUT and TMH of the subjects decrease (Table 3). There are significant differences in meiboscore and gland tortuosity within groups.

Age has significant influence on the majority parameters of ocular surface include gland tortuosity

As age increased, the OSDI and BMI percentile of subjects become higher and the BUT become smaller. And there are significant differences in gland tortuosity within three groups (Table 4).

The influence of BUT on meiboscore and OSDI score

In the group of BUT < 10s, the subjects have a larger percentage of meibomian gland atrophy and higher OSDI (Table 5).

Meibomian gland dysfunction was significantly correlated with BMI percentile within the same age group

The gland meiboscore was significantly correlated with BMI percentile in all three age groups. Additionally, gland tortuosity was significantly correlated with BMI percentile in the 13–15 years age group (Table 6). This suggests that the meiboscore and gland tortuosity worsen with an increase in BMI percentile within the same age group.

Table 3 Differences among five grades of BMI percentile

	0–20	20–40	40–60	60–80	80–100	*P*
N	63	18	38	33	48	
Age(years)	12.6	13.5	14.21	12.39	13.21	0.005
Gender(M/F)	29/34	5/13	16/22	15/18	27/21	0.323
BMI	15.5572	17.8378	19.5618	19.991	25.1672	< 0.001
OSDI	16.6635	19.0456	16.8121	18.0164	20.9629	0.499
BUT(s)	9.4646	10.8739	8.8529	7.6521	7.3535	0.024
TMH (mm)	0.1351	0.1344	0.1563	0.1967	0.1433	0.021
Meiboscore						
0	15	5	15	4	6	< 0.001
1	47	10	22	26	25	
2	1	3	1	3	13	
3	0	0	0	0	4	
Tortuosity						
0	9	3	9	8	4	0.036
1	46	13	28	21	30	
2	8	2	1	4	14	

BMI, body mass index; OSDI, ocular surface disease index; BUT, tear break-up time; TMH, tear meniscus height

Table 4 Differences among three stages of age (years)

	10–12	13–15	16–18	*P*
N	98	60	42	
Gender(M/F)	40/58	36/24	16/26	0.032
OSDI	15.66	20.51	20.64	0.033
BUT(s)	9.53	7.63	7.36	0.006
TMH (mm)	0.16	0.14	0.16	0.48
BMI percentile	42.43	49.68	70.48	< 0.001
Meiboscore				
0	24	10	11	0.677
1	63	42	25	
2	10	7	4	
3	1	1	2	
Tortuosity				
0	22	7	4	0.032
1	64	41	33	
2	12	12	5	
BMI percentile ranking				
1	32	26	5	< 0.001
2	9	2	7	
3	10	17	11	
4	22	6	5	
5	25	9	14	

BMI, body mass index; OSDI, ocular surface disease index; BUT, tear break-up time; TMH, tear meniscus height

Table 5 Differences between two levels of BUT

	BUT < 10s	BUT ≥ 10s	*P*
N	141	59	
Age(years)	13.13	13.02	0.931
Gender(M/F)	72/69	20/39	0.026
OSDI	19.57	14.80	< 0.001
TMH (mm)	0.15	0.16	0.607
BMI percentile	53.19	43.90	0.814
Meiboscore			
0	24	21	0.041
1	98	32	
2	16	5	
3	3	1	
Tortuosity			
0	22	11	0.503
1	96	42	
2	23	6	
BMI percentile ranking			
1	42	21	0.043
2	8	10	
3	27	11	
4	26	7	
5	38	10	

BMI, body mass index; OSDI, ocular surface disease index; BUT, tear break-up time; TMH, tear meniscus height

Correlation analysis between meibomian gland architecture and other parameters

The meiboscore of the glands was significantly correlated with weight, OSDI score, BUT, BMI percentile, and BMI percentile ranking ($P < 0.05$,Table 7). Furthermore, gland tortuosity was significantly correlated with weight, BMI percentile, and OSDI score ($P < 0.05$, Table 7). Therefore, weight and BMI percentile significantly influence the occurrence of MGD.

Table 6 Correlation analysis between meibomian gland architecture and BMI percentile within three stages of age (years)

		10-12y	13-15y	16-18y
N		98	60	42
meiboscore	spearman	0.228	0.342	0.46
	P	0.024	0.008	0.002
tortuosity	spearman	0.108	0.313	0.267
	P	0.291	0.015	0.088

BMI, body mass index; OSDI, ocular surface disease index; BUT, tear break-up time; TMH, tear meniscus height

Table 7 Correlation between meibomian gland structure and other parameters

	meiboscore		tortuosity	
	Spearman	*P*	Spearman	*P*
Age (years)	0.004	0.952	0.038	0.591
Gender	-0.021	0.769	-0.015	0.833
Weight (kg)	0.149	0.035	0.127	0.073
Height (cm)	0.002	0.981	0.068	0.335
OSDI	0.216	0.002	0.189	0.007
BUT(s)	-0.246	< 0.001	-0.109	0.124
TMH (mm)	-0.078	0.272	-0.156	0.027
BMI percentile	0.284	< 0.001	0.14	0.049
BMI percentile ranking	0.270	< 0.001	0.114	0.109

BMI, body mass index; OSDI, ocular surface disease index; BUT, tear break-up time; TMH, tear meniscus height

Table 8 Regression analysis of Meiboscore and significant correlated parameters

	meiboscore	
	r	*P*
OSDI	0.151	0.033
BUT	-0.165	0.020

OSDI, ocular surface disease index; BUT, tear break-up time

Regression analysis of meibomian gland structure and significant correlated parameters

The meiboscore of the glands was significantly influenced by the OSDI score and BUT in the regression analysis ($P < 0.05$, Table 8). However, no significant influencing factors for gland tortuosity were identified in the regression analysis.

Discussion

Currently, there are limited studies on indicators related to MGD or DED in children. In contrast, Wu et al. reported that the mean meiboscore for children aged 3–18 years in China was 0.39 ± 0.7 [20]. Additionally, other studies have reported that 42% of patients showed evidence of meibomian gland atrophy on meibography, while 37% exhibited varying degrees of gland tortuosity among American children and adolescents aged 4–17 years [21].

Our study utilized a large sample size to examine the impact of various factors, including age, weight, gender, BMI percentile, and others, on the meiboscore of the glands, gland tortuosity, and dry eye disease (DED). Consequently, 155 children (77.5%) had a meiboscore > 0, and 167 children (83.5%) exhibited a gland tortuosity score > 0. The proportion of abnormal meibomian gland structure was higher than in previous studies, which may be attributable to regional and ethnic differences.

Dyslipidemia and obesity have been shown to be associated with MGD in adults and obesity mouse model [3, 22]. Further investigation revealed that a high-fat diet led to decreased PPAR-γ expression and activated the MAPK and NF-κB signaling pathways, ultimately resulting in meibomian gland inflammation and dysfunction in mice [23]. And tear film instability associated with MGD is frequently observed in individuals with polycystic ovary syndrome (PCOS) characterized by elevated testosterone levels, as well as in those with a high BMI [24]. With the alteration of dietary structure and nutritional intake, the risk of obesity among Chinese children has gradually increased [11, 25]. Therefore, we hypothesized that malnutrition, as indicated by elevated BMI, may affect the structure of the meibomian gland in Chinese children. Additionally, we propose that maintaining adolescents' BMI percentile within the ideal range through appropriate dietary and lifestyle interventions could have beneficial effects on meibomian gland structure, primarily reflected in ocular surface parameters. Finally, our study demonstrated that weight and BMI percentile significantly influenced the structural parameters of the meibomian gland in Chinese children. This finding is consistent with previous studies, where higher BMI percentiles were significantly associated with increased meibomian gland tortuosity [9]. Meanwhile, age significantly influences most parameters of the ocular surface, including gland tortuosity. These results may be attributed to environmental deterioration and prolonged digital device usage. Additionally, patients with a BUT of less than 10 s exhibited higher meiboscores and OSDI scores. However, gender did not have a significant effect on meiboscore or gland tortuosity. More importantly, the gland meiboscore was significantly correlated with weight, OSDI score, BUT, BMI percentile, and BMI percentile ranking. Furthermore, gland tortuosity was significantly correlated with weight, BMI percentile, and OSDI score. It is plausible that patients with higher BMI percentiles may experience alterations in their systemic lipid profiles, which could influence the concentration of lipids in meibum. Subsequent changes in meibum viscosity may result in increased gland plugging and obstruction, thereby initiating a cascade leading to gland tortuosity and eventual dropout [6, 26]. In summary, childhood overweight affects the structure of the meibomian glands via abnormal lipid metabolism, inflammatory responses, hormonal changes, mechanical compression, lifestyle factors, and neuroendocrine dysregulation. These effects may result in gland dysfunction and contribute to ocular conditions, including DED.

There are several limitations in our study. First, a larger sample will provide a more representative result. Second, long-term longitudinal follow-up is needed to explore the changes of gland meiboscore and tortuosity in growth and development of children and to verify the effects of weight gain on meibomian glandular structure. Thirdly, despite the lack of a statistically significant correlation between age and meibomian gland structure in the correlation analysis, the potential influence of age on meibomian gland function cannot be entirely ruled out. Finally, whether actively modifying diet and lifestyle to maintain BMI percentile of adolescents within the ideal range can enhance the structure of the meibomian gland requires further investigation.

In conclusion, we evaluated the meiboscore, tortuosity, and other DED-related parameters in a substantial pediatric cohort. The meiboscore worsened with increasing weight, OSDI score, BMI percentile, and decreasing BUT, while gland tortuosity became more pronounced with increasing weight, BMI percentile, and OSDI score. There was a clear association between meibomian gland anomalies and higher BMI percentiles. Therefore, it is imperative to focus on the impact of overweight on meibomian gland structure and promptly adjust dietary habits and lifestyle to maintain the BMI percentile of adolescents within an optimal range, thereby reducing the risk of MGD in pediatric patients.

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None.

Author contributions
Design of the study (ZX, JM); Conduct of the study, data collection, analysis and interpretation (ZX, LB, JM, HY); Manuscript preparation and review (ZX, LB, JM, XW).

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was approved by the Institutional Review Board/Ethics Committee of Yongkang Hospital (LL202206). The data are anonymous, and the requirement for informed consent was therefore waived by the Institutional Review Board/Ethics Committee of Yongkang Hospital.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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