Prevalence, ethnic differences and risk factors of primary angle-closure glaucoma in a multiethnic Chinese adult population: the Yunnan Minority Eye Study

Ying Wang, Qing Cun, Jun Li, Wei Shen, Wen-Yan Yang, Yi-Jin Tao, Zhi-Qiang Niu, Ying Zhang, Hua Zhong, Chen-Wei Pan

ABSTRACT

Purpose To describe the prevalence and risk factors of primary angle-closure glaucoma (PACG) and to explore nationality difference in Chinese.

Methods The Yunnan Minority Eye Study was conducted in a rural multiethnic area in Yunnan province and included 6546 participants aged over 50 years. PACG was diagnosed based on International Society of Geographical and Epidemiologic Ophthalmology criteria by experienced ophthalmologists. Multivariate regression modelling was conducted to examine risk factors for PACG. Principal component analysis (PCA) was performed to evaluate the effects of ethnicity on PACG.

Results The overall prevalence of PACG was 0.7% (95% CI: 0.5% to 0.9%). PCA indicated that ethnicity is significantly related to the presence of PACG (p<0.001) after controlling for other risk factors. In addition, higher PACG prevalence was also correlated with older age (60–69 years group (OR: 3.47; 95% CI: 1.11 to 10.84; P<0.001) and 70–79 years group (OR: 1.40 to 15.86; p<0.05) as compared with 50–59 years group), higher intraocular pressures (OR: 1.26; 95% CI: 1.17 to 1.36; p<0.05) and shorter axial lengths (OR: 0.42; 95% CI: 0.32 to 0.56; p<0.001) and thinner central corneal thicknesses (OR: 0.89; 95% CI: 0.81 to 0.99; p<0.05).

Conclusions This multiethnic study on Chinese adults living in the same geographical location indicated that ethnicity is a significant risk factor for PACG. However, there were still some of the effects of ethnic differences on the prevalence of PACG that could not be explained and further studies should take culture and lifestyle factors into account.

INTRODUCTION

Primary angle-closure glaucoma (PACG) is a major cause of irreversible blindness, affecting about 17 million people all over the world.1 It was reported that Asia accounted for 71.76% of the current estimated PACG cases worldwide1 and the PACG burden has estimated to be the highest in east Asia.2 While the prevalence of PACG is lower than that of primary open-angle glaucoma (POAG) in the Chinese population, PACG carries an increased risk of severe, bilateral visual impairment than POAG3–4 and thus poses a significant financial burden. However, visual loss resulting from PACG is potentially preventable if operative treatment is performed in the early stage,5 which establishes a need for the early diagnosis and treatment of PACG.

As the imbalance of social and economic development, there are great differences in the prevalence of various eye diseases, blindness and risk factors. Recent research has demonstrated that people with lower socioeconomic status tend to have less eye care visits, less glaucoma awareness and higher odds of having end-stage glaucoma, causing higher glaucoma medication expenses.6–8 Therefore, understanding how prevalent PACG is in an area with a low level of economic development in China is essential to public health planning and reasonable allocation of resources. In addition, PACG is regarded to be affected by inherited genes and environmental exposures.9–11 China is a multi-ethnic country with a large population and there are disparities in cultures and lifestyles among diverse ethnic groups, which may explain some of the prevalence differences in PACG. However, few studies have included analysis of different ethnic minorities.

Although several prevalence surveys on PACG have been conducted in north and south of China,12–14 the knowledge of the ethnic differences in PACG in Chinese population remains scarce. The Yunnan province is located in the southwest of China and has a population of 45.96 million, where the per capita gross domestic product is less than one-third of the country’s average and has a heterogeneous population consisting of 25 minority ethnicities, which is a good choice to observe ethnic differences in diseases. The multiethnic population representing three major ethnic groups residing in the same geographical location provides a unique opportunity to study this. The aim of this study was to describe the prevalence and risk factors of PACG and to determine if ethnicity is associated with PACG among Chinese adults.

METHODS

Study population

The Yunnan Minority Eye Study is a population-based study on multiethnic adults aged 50 years or older living in in Yunnan province located in

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have been reported before. 17–20 Body weight and height were measured with participants wearing light and thin clothing and without shoes using a wall-mounted tape and a digital scale, respectively. Body mass index (BMI) was calculated using the formula ((weight in kg)/(height in m²). Blood pressure (BP) was measured three times or more in a 5 min interval using a standardized mercuric-column sphygmomanometer. The data of 8174 enumerated individuals completed the glaucoma screening procedure and were available for analysis, including 2133 (77.8% response rate) Bai, 2208 (80.5% response rate) Yi and 2205 (82.0% response rate) Han Chinese.

Clinical examination and questionnaires

All clinical examinations and questionnaires were completed by trained personnel, and detailed examination procedures were described elsewhere.17–20 In brief, a random cluster sample of Bai, Yi and Han adults aged 50 years or older were invited to participate in the study based on the official records. We excluded ineligible individuals who had moved from the residing address, or had not been living there for more than 6 months, or were deceased. Eventually, 6546 participants of the total 8174 enumerated individuals completed the glaucoma screening procedure and were available for analysis, including 2133 (77.8% response rate) Bai, 2208 (80.5% response rate) Yi and 2205 (82.0% response rate) Han Chinese.

### Table 1

Prevalence of primary angle-closure glaucoma by age, sex and ethnicity

| Group            | Age | All          | Men          | Women         |
|------------------|-----|--------------|--------------|---------------|
|                  |     | n  | Cases | Prevalence (95% CI) | n | Cases | Prevalence (95% CI) | n | Cases | Prevalence (95% CI) |
| Bai Chinese      |     | 716| 0  | 0.0 (–) | 220 | 0 | 0.0 (–) | 496 | 0 | 0.0 (–) |
|                  | 60–69| 775| 10 | 1.3 (0.5 to 2.1) | 308 | 2 | 0.6 (0.0 to 1.6) | 467 | 8 | 1.7 (0.5 to 2.9) |
|                  | 70–79| 524| 7  | 1.3 (0.4 to 2.3) | 202 | 1 | 0.5 (0.0 to 1.5) | 322 | 6 | 1.9 (0.4 to 3.3) |
|                  | ≥80 | 118| 3  | 2.5 (0.0 to 5.4) | 39  | 0 | 0.0 (–) | 79  | 3 | 3.8 (0.0 to 8.0) |
| Crude total      |     | 2133|20| 0.9 (0.5 to 1.4) | 769 | 3 | 0.4 (0.0 to 0.8) | 1364| 17| 1.2 (0.7 to 1.8) |
| Adjusted total*  |     | 0.7 (0.3 to 1.2) | | | | | | | |
| Yi Chinese       |     | 687| 3  | 0.4 (0.0 to 0.9) | 282 | 0 | 0.0 (–) | 405 | 3 | 0.7 (0.1 to 1.6) |
|                  | 60–69| 813| 4  | 0.5 (0.0 to 1.0) | 358 | 2 | 0.6 (0.0 to 1.3) | 455 | 2 | 0.4 (0.0 to 1.0) |
|                  | 70–79| 567| 6  | 1.1 (0.2 to 1.9) | 238 | 0 | 0.0 (–) | 329 | 6 | 1.8 (0.4 to 3.3) |
|                  | ≥80 | 141| 0  | 0.0 (–) | 72  | 0 | 0.0 (–) | 69  | 0 | 0.0 (–) |
| Crude total      |     | 2208|13| 0.6 (0.3 to 0.9) | 950 | 2 | 0.2 (0.0 to 0.5) | 1258| 11| 0.9 (0.4 to 1.4) |
| Adjusted total*  |     | 0.4 (0.1 to 0.7) | | | | | | | |
| Han Chinese      |     | 709| 1  | 0.1 (0.0 to 0.4) | 247 | 0 | 0.0 (–) | 462 | 1 | 0.2 (0.0 to 0.6) |
|                  | 60–69| 755| 4  | 0.5 (0.0 to 1.0) | 306 | 3 | 1.0 (0.0 to 2.1) | 449 | 1 | 0.2 (0.0 to 0.7) |
|                  | 70–79| 562| 7  | 1.2 (0.3 to 2.2) | 252 | 3 | 1.2 (0.0 to 2.5) | 310 | 4 | 1.3 (0.0 to 2.6) |
|                  | ≥80 | 179| 1  | 0.6 (0.0 to 1.6) | 79  | 0 | 0.0 (–) | 100 | 1 | 1.0 (0.0 to 3.0) |
| Crude total      |     | 2205|13| 0.6 (0.3 to 0.9) | 884 | 6 | 0.7 (0.1 to 1.2) | 1321| 7 | 0.5 (0.1 to 0.9) |
| Adjusted total*  |     | 0.4 (0.1 to 0.7) | | | | | | | |
| All ethnic groups<60 | 2112| 4  | 0.2 (0.0 to 0.4) | 749 | 0 | 0.0 (–) | 1363| 4 | 0.3 (0.0 to 0.6) |
|                  | 60–69| 2343|18 | 0.8 (0.4 to 1.1) | 972 | 7 | 0.7 (0.2 to 1.2) | 1371| 11| 0.8 (0.3 to 1.3) |
|                  | 70–79| 1653|20 | 1.2 (0.7 to 1.7) | 692 | 4 | 0.6 (0.0 to 1.1) | 961 | 16| 1.7 (0.9 to 2.5) |
|                  | ≥80 | 438| 4  | 0.9 (0.0 to 1.8) | 190 | 0 | 0.0 (–) | 248 | 4 | 1.6 (0.0 to 3.2) |
| Crude total      |     | 6546|46| 0.7 (0.5 to 0.9) | 2603| 11| 0.4 (0.2 to 0.7) | 3943| 35| 0.9 (0.6 to 1.2) |
| Adjusted total*  |     | 0.5 (0.3 to 0.7) | | | | | | | |

*Adjusted prevalence rates are based on the 2010 China National Census of Yunnan province.

southwestern rural of China in the study period from 2010. The details of this cohort have been described elsewhere.17–20 In brief, a random cluster sample of Bai, Yi and Han adults aged 50 years or older were invited to participate in the study based on the official records. We excluded ineligible individuals who had moved from the residing address, or had not been living there for more than 6 months, or were deceased. Eventually, 6546 participants of the total 8174 enumerated individuals completed the glaucoma screening procedure and were available for analysis, including 2133 (77.8% response rate) Bai, 2208 (80.5% response rate) Yi and 2205 (82.0% response rate) Han Chinese.

### Clinical examination and questionnaires

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### Diagnostic definitions

Glaucoma was diagnosed according to the criteria described by International Society of Geographical and Epidemiologic Ophthalmology based on three categories,22 which was in line with the previous study.20 Eyes had optic disc and visual field abnormalities (VCDR or asymmetry 97.5th percentile) with glaucomatous visual field defect were divided into category 1. Category 2 required a severely damaged optic disc (VCDR or asymmetry 99.5th percentile for the normal population) if an adequate visual field test was of absence. In category 3, eyes with the condition of a visual acuity<3/60 and an IOP exceeding the 99.5th percentile for the normal population or evidence of previous glaucoma filtering surgery were included. Based on that definition, PACG was defined as glaucoma with occlusive anterior chamber angles during gonioscopy. Final adjudication of PACG cases was made by a glaucoma specialist (HZ). The non-glaucomatous subjects (control group) were those who did not have any type of glaucoma or were not glaucoma suspects.

Cataract was assigned when lens opacity was observed in either eye using a slit lamp according to the Lens Opacities Classification System III.23 Hypertension was defined as BP of 140/90 mm Hg or higher or use of antihypertensive medication.
Statistical analyses

Prevalence was calculated on an individual who had at least one eye diagnosed with PACG. Of the 6546 individuals, subjects missing the inclusion and exclusion criteria or without complete data on interviewer-administered questionnaires and examination were excluded from further analysis. Considering the inter-eye correlation on ocular biometric parameters (r>0.6 for all) and the results from two eyes are similar, the related comparisons were performed by using data of the right eye. When the right eye was aphakic or pseudophakic due to previous cataract surgery, or has missing data, the other eye was selected. In the statistical description, mean and SD were used for normally distributed variables, and number and percentage were used to express categorical variables. The differences of baseline characteristics between PACG and non-PACG groups were evaluated by t-test for normally distributed variables, univariable test of Mann-Whitney for skewed variables and χ² test for categorical variables. Multivariate logistic regression models were fitted to estimate the ORs of selected risk factors. Further, we used the backward stepwise algorithm by Akaike information criterion to find the prediction model (model 2). In addition, in order to evaluate the effect of ethnicity on PACG, we performed principal component (PC) analysis (PCA) to adjust the potential relationship between ethnicity and other significant risk factors (based on model 1). The number of PCs was extracted according to the criteria with an eigenvalue greater than 1. The likelihood ratio test was used to assess the residual effects of ethnicity unexplained from the selected risk factors.

Statistical analyses were all performed using SPSS V.24.0 (SPSS). Statistical difference was considered to be significant at the level of 0.05.

RESULTS

A total of 6546 participants were included in this study and the response rate was 80.1%, including 2133 Bai Chinese, 2208 Yi Chinese and 2205 Han Chinese. No age and sex differences were observed between participants and non-participants (p>0.05). Table 1 presents the prevalence estimate of PACG for the whole cohort and in age-stratified, sex-stratified and nationality-stratified groups. Prevalence rates were standardised to the population distribution from the 2010 China National Census of Yunnan province. The total crude prevalence of PACG was 0.7% (95% CI, 0.5% to 0.9%), which was found in 0.4% (95% CI, 0.2% to 0.7%) of men and 0.9% (95% CI, 0.6% to 1.2%) of women. The prevalence of PACG increased with age though there was a fall in people at 80 years or more (0.9%, 95% CI: 0.0 to 1.8) as compared with 70–79 years group (1.2%, 95% CI: 0.7 to 1.7). A similar trend was observed in women, while the peak prevalence of PACG in men appears in the age group from 60 to 69 years. Of the three ethnic groups, Bai Chinese had a higher prevalence of PACG (0.9%; 95%CI: 0.5% to 1.4%) than Yi and Han Chinese (both 0.6%; 95%CI: 0.3% to 0.9%).

The sociodemographic and important ophthalmic examination index characteristics of the respondents are shown in table 2. After excluding participants with previous cataract surgery or missing data, 6069 individuals were considered eligible for further analyses. The mean (SD) age was 64.74 (9.11) years and 60.78% were women. The prevalence of PACG showed a significant statistical association with age and cataract (p<0.05). Bai, Yi and Han Chinese comprised 32.69%, 33.71% and 33.60% of the whole population, respectively, and comparing the prevalence of PACG did not reveal major differences in ethnicity distribution (p=0.22). In addition, the prevalence of PACG was not significantly correlated with the systemic parameters of sex, education level, marital status, smoking (former or current), alcohol consumption, BMI and hypertension (p>0.05). Furthermore, we performed an analysis for ophthalmological parameters and found that higher prevalence of PACG was associated with higher IOPs, thinner CCTs, higher VCDRs and shorter ALs (p<0.05 for all). In figure 1 we also display the distribution of the important ocular biometric parameter in the comparison between PACG patients and non-PACG participants, visualised as the boxplots.

To further explore the effect of potential risk factors on PACG, we performed the multivariable analysis and results are shown in table 3. In model 1, age, gender, education level, ethnicity, cataract, hypertension and important ophthalmological biological parameters (IOP, AL, ACD and CCT) remained based on univariate analysis results (p<0.10) or scientific significance. After adjustment, a higher PACG prevalence was correlated with
older age (expect people aged over 80), ethnicity (Bai Chinese vs Han Chinese), higher IOPs, shorter ALs and thinner CCTs. However, sex, education, hypertension, cataract and ACD were not associated with the PACG prevalence (all p > 0.05). Further, using the backward stepwise regression method, we established a prediction model for PACG. The receiver operator characteristic curve was carried out to assess the predictive effectiveness of the risk factors in model 1 and to discover an optimal cut-off point according to the maximum corresponding specificity and sensitivity. Finally, model 2 with the area under the curve value of 0.856 was recognised as the best prediction model, with sensitivity of 70% and specificity of 90%. This model indicated that the combination of risk factors including age, ethnicity, cataract, IOP, AL and CCT was a good predictor for PACG outcome (p < 0.05 for all).

Table 4 demonstrates the relative proportion of variance explained by the effect of ethnicity and PCs (other important factors in model 1) on PACG. As a result, the PCA model could explain 70.4% of total variability of the selected risk factors with five PCs extracted. After adjusting for the PCs, we observed that the effect of ethnicity remained statistically significant on PACG prevalence (p < 0.001).

DISCUSSION
This multiethnic study included a representative sample of three major ethnic groups living in rural Yunnan province. The prevalence of PACG in this study is similar to the estimated prevalence in Asia and lower than that reported in other studies in China. In multivariable analysis, higher PACG prevalence was correlated with older age, Bai Chinese, higher IOPs, shorter ALs and thinner CCTs. The ethnicity difference was supported by PCA, which revealed that ethnicity is significantly related to the presence of PACG after controlling for other risk factors.

Population-based studies have presented a wide range of PACG prevalence, varying from 0.18% in people living in Singapore to 4.32% in south India. The prevalence of PACG in our study is consistent with recent estimates of the overall PACG pooled prevalence in Asia (0.7%, 95% CI: 0.6% to 1.0%). After calibrating the age of the study population to 50 years and older, the prevalence of PACG we observed was still lower than those reported in previous investigations on study populations living in northern and southern China, with the highest PACG prevalence found in Northeast China (figure 2). The reasons for the regional discrepancy in prevalence may contribute to genetic factors, environmental exposures or study methodology.

Racial differences in glaucoma have been reported in previous studies. However, few studies have assessed variations in the prevalence of PACG among different ethnicities. In this study, we observed that Bai Chinese were more likely to develop PACG compared with Han and Yi Chinese. This finding has an important implication, because the deviation of PACG prevalence in three ethnicities may indicate that more concern should be paid on Bai population in local health policies in the
future. Since the genetic difference may be relatively smaller among different ethnic groups living in the same geographical location, the variation of demographic factors and health condition may explain some of the ethnic difference in the observed ethnic differences in PACG prevalence. To examine how much the ethnicity factor contributes to the prevalence of PACG, PCA was performed, which was used to control for confounding and correlation among these confounders. In this study, we found that ethnicity was still a significant factor associated with PACG after controlling for the other risk factors based on the selected model and the ethnicity factor contributes to the prevalence of PACG, PCA adjusted for age, ethnicity, AL, IOP, CCT and cataract. A previous large population-based study has demonstrated asso-
ciated factors were included in the model. Model 2 adjusted for age, ethnicity, AL, IOP, CCT and ACD. Model 2 adjusted for age, ethnicity, AL, IOP, CCT and ACD.

### Table 3 Multiple regression analyses for potential risk factors for primary angle-closure glaucoma in the Yunnan Minority Eye Study

| Age group (years) | Model 1 | | Model 2 | |
|------------------|---------|---|---------|---|
|                   | OR (95% CI) | P | OR (95% CI) | P |
| <60              | Ref. | | Ref. | |
| 60–69            | 3.47 (1.11 to 10.84) | <0.05 | 3.33 (1.07 to 10.37) | <0.05 |
| 70–79            | 4.71 (1.40 to 15.86) | <0.05 | 4.09 (1.26 to 13.30) | <0.05 |
| ≥80              | 3.85 (0.76 to 19.47) | 0.10 | 3.32 (0.68 to 16.19) | 0.14 |
| Sex              |         |   |         |   |
| Men              | 1.61 (0.69 to 3.75) | 0.27 | |
| Women            | Ref. | | Ref. | |
| Ethnicity        |         |   |         |   |
| Bai Chinese      | 2.82 (1.07 to 7.44) | <0.05 | 2.89 (1.22 to 6.86) | <0.05 |
| Yi Chinese       | 1.54 (0.63 to 3.78) | 0.35 | 1.53 (0.62 to 3.76) | 0.36 |
| Han Chinese      | Ref. | | Ref. | |
| Education        |         |   |         |   |
| Formal           | 1.24 (0.59 to 2.63) | 0.56 | |
| Informal         | Ref. | | Ref. | |
| Hypertension     |         |   |         |   |
| Yes              | 0.76 (0.39 to 1.50) | 0.43 | |
| No               | Ref | | Ref | |
| Cataract         |         |   |         |   |
| Yes              | 2.16 (0.87 to 5.34) | 0.10 | 2.10 (0.85 to 5.18) | 0.11 |
| No               | Ref | | Ref | |
| IOP (1 mm Hg higher) | 1.26 (1.17 to 1.36) | <0.001 | 1.25 (1.16 to 1.35) | <0.001 |
| AL (1 mm longer) | 0.42 (0.32 to 0.56) | <0.001 | 0.42 (0.32 to 0.54) | <0.001 |
| CCT (10 µm thinner) | 0.89 (0.81 to 0.99) | <0.05 | 0.89 (0.80 to 0.98) | <0.05 |
| ACD (1 mm longer) | 1.00 (0.50 to 1.99) | 0.99 | |

OR (95% CI) P OR (95% CI) P

Model 1 adjusted for age, sex, ethnicity, education, hypertension, cataract, IOP, AL, CCT and ACD.

Model 2 adjusted for age, ethnicity, AL, IOP, CCT and ACD.

ACD, anterior chamber depth; AL, axial length; CCT, central corneal thickness; IOP, intraocular pressure.

### Table 4 Principal component (PC) analysis to study the potential relationship between ethnicity and other significant associated factors

| Ethnicity | PCs |
|-----------|-----|
| Pooled effect | 17.14 | 71.08 |
| P value* | <0.001 | <0.001 |
| Cumulative PC proportion (n) | 0.704 (5) |

Pooled effects were estimated as the differences of the likelihood ratio (LR) test values between the overall model and the model removing the corresponding variables.

Risk factors included in principal component analysis are selected based on model 1.

*LR test.

n, number of principal components.

Figure 2 Prevalence of primary angle-closure glaucoma defined by International Society of Geographical and Epidemiologic Ophthalmology criteria in population-based studies in China. The bubble colour indicates different studies and the bubble size represents the size of the study population.

selected factors. Thus, we were unable to adequately control for the effects of exposure to other risk factors on ethnic differences. It is likely that the unexplained or undiscovered risk factors such as culture and lifestyle that may have a significant impact on PACG development and further studies are warranted.

With regard to other risk factors, increasing age has often been identified as an increased risk of PACG, which is consistent with our study. Our study also confirmed the association of several ocular parameters including higher IOP, thinner CCT and shorter AL with PACG, which have been reported previously in other studies. In addition, the effect of systemic factors on development of PACG also was evaluated in this study and we found only a weak association between cataract and PACG. A previous large population-based study has demonstrated associations between PACG and different systemic comorbidities, including cataract, hyperlipidemia, headaches, liver diseases and peptic ulcers, of which cataract is regarded as the strongest risk factor. Thus, it has to be taken into account that the association between PACG and cataract has yet to be established firmly in current studies. The reasons for this result may be the history of cataract surgery in different groups or other confounding factors such as LT. Previous observations have described the relationship between increasing risks of cataract and thinner lenses, which could be explained by a greater rate of condensation of lens material and increasing dehydration in the nucleus of lenses with cataract. However, participants with PACG tended to have thicker lens as compared with their non-PACG counterparts, though this association was not statistically significant, which might weaken the relationship between cataract and PACG.

Several limitations should be mentioned here. The first limitation came from unresponsive people. Although our study showed no age or sex differences between participants and non-participants, there may be other important differences that could cause selection bias for prevalence estimation. Meanwhile, excluding subjects with incomplete data can also bias the result of risk factor exploration. Second, the effect of other risk factors such as cultures and lifestyles that could explain remaining ethnic difference on PACG outcome have not been well established yet. Third, one should note that the cumulative contribution of the five PCs encompassing the heterogeneity among three ethnicities in this model accounts for 70.4%.
Therefore, there is still some variability of parameters not be included, leading to residual confounding that may contribute to the ethic differences observed. Fourth, this study is a cross-sectional design that limited the ability to determine causality and we could not explore the relationship between dynamic changes of related parameters and the onset of PACG. It has been suggested that IOP variability between visits could be a more important predictor for glaucoma progression than the mean IOP.10

In conclusion, the crude PACG prevalence of this ethnically mixed rural population from Yunnan province with an age over 50 years was 0.7%, which was lower than previous studies performed on populations from other regions of China. This study revealed a significant ethnic difference in the prevalence of PACG. In addition, a higher prevalence of PACG is related to older age, higher IOPs, shorter ALs and thinner CCTs. These results might add accumulating evidence for further study to explore the mechanism of the development of PACG and have some implications regarding the prevention of PACG among the older population.

Contributors Study conception and design: C-WP and HZ. Material preparation and data collection: QC, JL, WS, W-YY, Y-JT, Z-QN, YZ and HZ. Data analysis: YW. Drafting of the manuscript: YW and QC. Critical revision of the manuscript for important intellectual content: C-WP. All authors read and approved the final manuscript. C-WP accepts full responsibility for the work and the conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests None declared.

Patient consent for publication Participants gave informed consent to participate in the study before taking part.

Ethics approval This study was approved by the Kunming Medical University Ethics Review Board (reference number 2013084566) and was conducted in accordance with the tenets of the World Medical Association’s Declaration of Helsinki.

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Data availability statement No data are available.

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