

Association between dry eye and traditional Chinese medicine body constitutions

A Taiwanese adults study

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Abstract

In the theory of traditional Chinese medicine (TCM), except for the balanced constitution, other constitutions are unbalanced and may lead to susceptibility to certain diseases. This study made the first efforts to explore the relationship between TCM constitutions and the dry eye condition.

This cross-sectional study collected information from 2760 subjects aged 30 to 70 years who had participated in a questionnaire survey conducted by Taiwan Biobank (TWB) in 2012 to 2017. The questionnaire included questions on basic demographic characteristics, chronic diseases, depression, blood lipid levels, lifestyles, and drug allergies, as well as a TCM constitution scale developed by a research team of TCM constitution and syndrome at China Medical University College of Chinese Medicine.

Unadjusted and stratified multiple logistic regression analyses were performed to explore the relationships between TCM constitutions and dry eye. The analysis revealed that subjects falling into the constitution category of Yang deficiency, Yin deficiency, or Phlegm stasis were more likely to develop dry eyes (crude odds ratio [OR]=1.741, 95% confidence interval [CI]=1.361–2.227; crude OR=2.4821, 95% CI=1.968–3.131; and crude OR=2.082, 95% CI=1.597–2.714, respectively). After adjusting for important risk factors (demographic characteristics, chronic diseases, blood lipid levels, lifestyles, depression, and drug allergies), subjects with an unbalanced constitution were 1.6 to 2.5 times more likely to develop dry eye than those with a balanced constitution.

These results confirm a high correlation of TCM constitution with dry eye. Considering that the current treatment outcome is not fully satisfactory to the patients with dry eyes, integration of TCM and Western medicine may be an alternative treatment option. Individualized treatments and lifestyle recommended should be provided to patients with different TCM constitutions to alleviate dry eye symptoms.

Abbreviations: AOR = adjust odds ratio, BCQ = Body Constitution Questionnaire, BMI = body mass index, CCMQ = Constitution in Chinese Medicine Questionnaire, CI = confidence interval, HbA1C= glycated hemoglobin, HDL = high-density lipoprotein, ICC = intra-group correlation coefficients, IOP = increased intraocular pressure, LDL = low-density lipoprotein, OR = odds ratio, SD = standard deviation, TC = total cholesterol, TCM = traditional Chinese medicine, TG = total triacylglyceride, TWB = Taiwan Biobank.

Keywords: dry eye, keratoconjunctivitis sicca, traditional Chinese medicine, traditional Chinese medicine constitution

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1. Introduction

Dry eye, also known as keratoconjunctivitis sicca, is a multifactorial ocular surface disease. It is one of the most common eye diseases, with the global prevalence in adults ranging between 5% and 50%.^[1] The prevalence of dry eye in Taiwan is 4.87% and the probability of developing dry eye is 2.34-fold higher in women than that in men.^[2] Dry eye is characterized by eye dryness, itching, redness, photophobia, and blurred vision.^[3] It can also reduce patient's productivity and degrade quality of life.^[3] Moreover, frequent return visits to clinics and administration of multiple medications may cause an economic burden on patients with dry eyes.^[3] Economic statistics from the US indicate that the average annual cost of treating dry eye is about \$780 per patient and the annual total treatment burden for dry eye disease is about \$3.8 billion.^[4] Furthermore, with the increasing use of electronic products in recent decades, dry eye has plagued hundreds of millions of people and become an urgent public health issue.^[5]

Dry eye originates from a loss of homeostasis of the tear film, which leads to tear's hyperosmolarity and instability.^[1] The hyperosmolarity and instability, as well as inflammatory reactions on the ocular surface are often considered triggers for the vicious cycle of dry eye. Dry eye treatments include medications (supplemented with artificial tear) and non-medications (e.g., lifestyles and environment modification) as well as punctual occlusion with plugs as adjuvant therapy. Severe cases with poor clinical treatment response may require autologous serum eye drops and therapeutic soft contact lenses.^[6] Despite the various treatments for dry eye, treatment outcome is not satisfactory for all the dry eye patients. Nearly 20% of dry eye patients, with a higher proportion of women than men, report dissatisfaction after treatment.^[7] Thus, an increasing number of patients seeking alternative and complementary medicines such as the traditional Chinese medicine (TCM) has been the trend in recent years.^[8]

A growing number of studies have explored the treatment of dry eye with TCM.^[3,9,10] Meanwhile, other studies have long observed differences in the TCM constitution between individuals, which suggests individualized treatment. The theory of TCM constitutions emphasizes that personal constitution changes with age from birth and affects personal life and health characteristics.^[11] The theory of TCM constitutions originates from the Yellow Emperor's Canon of Medicine 2000 years ago and describes innate and acquired body characteristics from four pairs of dualities: Yin-Yang, exterior-interior, cold-heat, and deficiency-excess, along with qi, blood, body fluids, and internal organs, elaborating on the characteristics of the whole body and the imbalanced states.^[11] The TCM constitution concept, which is intended to differentiate between individuals, systematically integrates the Yang deficiency constitution, Yin deficiency constitution, Phlegm stasis constitution, and balanced constitution, as well as other types of constitutions,^[11-17] and emphasizes the individuality of each patient, with a focus on restoring the patient's overall balance and harmony rather than only treating the illness.^[18] This study utilized the body constitution questionnaire (BCQ) which was developed in Taiwan. BCQ was developed to provide objective tools to meet scientific research requirements. The BCQ measures the psychological and physiological states of deviations in body constitution in each patient during the past month. It has been developed for the evaluation of the composition of Yin deficiency, Yang deficiency, and Phlegm stasis.^[12-16] The TCM constitution scale classifies the constitution into three types (Yin deficiency, Yang deficiency, and

Phlegm stasis), and all items are organized into three independent constitution types. So, with different constitutions exerting different influences on physiological characteristics, people are subject to different disease susceptibility and disease progression.^[11]

Western medicine often takes a reactive approach to treat diseases; that is, diagnoses and treatments are administered only after disease onsets. The TCM constitution theory states that only a balanced constitution represents a balanced and healthy body state, while all other constitutions are unbalanced body states that may result in a high susceptibility to some diseases.^[19] Identification of the TCM constitution is clinically beneficial to determine whether a patient is susceptible to certain diseases, such as dry eye, and such knowledge may even help prediction of patient's prognosis.^[20] However, to date, no research has been conducted to explore the relationship between TCM constitutions and dry eye. To fill this knowledge gap, we conducted this first study to explore the relationship between different Yang deficiency, Yin deficiency, Phlegm stasis, and dry eye, hoping to provide a proactive approach for prevention and management of this disease.

2. Materials and methods

2.1. Data source and sample

This cross-sectional study included 2760 subjects who participated in a questionnaire survey conducted by Taiwan Biobank (TWB), a national health database open to researchers,^[21] in 2012 to 2017. The TWB is the largest government-supported biobank in Taiwan. It is accessible to researchers and contains health information collected from Taiwan residents aged 30 to 70 years between 2008 and 2017. It aimed to build a nationwide research database that integrates genomic/epigenomic profiles, lifestyle patterns, dietary habits, environmental exposure history, and long-term health outcomes of 300,000 residents of Taiwan.^[21,22]

2.2. Instruments

The research data comprised basic demographic information (sex, age, education, marital status, residence status [living alone or not], education level, and work status), blood lipid levels (glycated hemoglobin [HbA1C], total cholesterol [TC], total triacylglyceride [TG], low-density lipoprotein [LDL], and high-density lipoprotein [HDL]), lifestyle information including personal health behaviors (alcohol consumption, smoking, betel nut consumption, and exercise habits) and dietary characteristics (tea, coffee, vegetarianism, and midnight snacks), drug allergy information, chronic systemic conditions (hyperlipidemia, hypertension, diabetes mellitus, and depression), ocular conditions (cataract, glaucoma, dry eye, retinal detachment, vitreous degeneration, and color blindness) and TCM constitution information. Blood lipid data were classified according to the guideline specified in the release notes of TWB^[21] as normal (HbA1C 4.6-6.4, TC < 200 mg/dL, TG < 150 mg/dL, LDL < 100 mg/dL, HDL > 40 mg/dL in men, and > 50 mg/dL in women) or abnormal (HbA1C > 6.4, TC ≥ 200 mg/dL, TG ≥ 150 mg/dL, LDL ≥ 100 mg/dL, HDL ≤ 40 mg/dL in men, and ≥ 50 mg/dL in women). The diagnosis of systemic and ocular diseases was made by all the participants' own specialists. The TCM constitution data was based on a survey using a BCQ designed by the research team of TCM constitution and syndrome led by Dr Yi-Chang Su

of China Medical University College of Chinese Medicine. The BCQ comprised 44 questions on three constitutions including Yang deficiency, Yin deficiency, and Phlegm stasis. Each question was constructed using appropriate frequency and intensity scale descriptors and scored using a 5-point Likert scale. Some items belonging to these 3 types overlapped with each other. If the total score of a subject satisfied the identification criterion of a constitution, the subject was considered to have that constitution. That is, if a patient scored 31 or more on the 19 Yang deficiency questions, the subject had Yang deficiency; if a patient scored 29.5 or more on the 19 Yin deficiency questions, the subject had Yin deficiency; and if a patient scored 27 or more on the 16 Phlegm stasis questions, the subject had Phlegm stasis. If the patient meets the criteria of more than 2 constitutions, it is called mixed body constitution. The Cronbach's α coefficients and intra-group correlation coefficients (ICC) for Yang deficiency, Yin deficiency, and Phlegm stasis were 0.88 and 0.91,^[12,13] 0.85 and 0.91,^[14,15] and 0.88 and 0.91,^[16] respectively.

2.3. Ethical approval

Recruitment of individuals in the TWB project conformed to the relevant regulations and guidelines. Before data collection, written informed consent was obtained from each participant, whose identity information was protected by encryption and conversion to a non-identifiable format and removing data links.^[21,22] After the study was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (VGHKS18-CT6-03), the TWB gave permission for this set of data to be used in this study.

2.4. Statistical analysis

The variables analyzed in the study included TCM constitutions (Yang deficiency, Yin deficiency, and Phlegm stasis), age, sex, marriage status, residence status (living alone or not), education level, employment, body mass index (BMI), drug allergies, chronic hyperlipidemia, hypertension, diabetes mellitus, depression, smoking, alcohol consumption, betel nut consumption, exercise, tea drinking, coffee drinking, vegetarianism, midnight snack, HbA1C, TC, TG, HDL, and LDL.

Continuous variables are presented as mean \pm standard deviation (SD) and categorical values, percentages. Independent *t* test and Pearson chi-square tests were used to assess the differences for continuous and categorical variables, respectively, to explore the correlation between TCM and other variables. Finally, stratified multiple logistic regression analysis was performed to determine whether Yang deficiency, Yin deficiency, and Phlegm stasis were independent predictors of dry eye:

1. the unadjusted odds ratios (ORs) were calculated and
2. the demographic characteristic, lifestyle, lipid profile, chronic disease, depression, and drug-allergy variables were sequentially included in the regression model.

Statistical analysis was performed using IBM SPSS Statistics (version 22.0, IBM Corp, Armonk, NY) software, where *P*-values < .05 were considered statistically significant.

3. Results

The 2760 subjects included in this study comprised 1423 females (51.6%) and 1337 males (48.7%), aged 30–70 years (average age

48.69 years, SD=10.072 years). Among the subjects, 507 (18.4%) were diagnosed with Yang deficiency (mean \pm SD: 36.66 \pm 6.091), 542 (19.6%) with Yin deficiency (mean \pm SD: 31.97 \pm 7.58), and 376 (13.6%) with Phlegm stasis (mean \pm SD: 32.29 \pm 5.51). Table 1 shows that the average age of subjects with Yin deficiency was higher than those of subjects with the other two constitutions. Among the female subjects, the number of those with Yang deficiency, Yin deficiency, or Phlegm stasis was higher than that of those with none of the above constitutions. Among the subjects with Yang deficiency and Phlegm stasis, 23.7% and 24.0%, respectively, were unmarried. A higher proportion of subjects with Yang deficiency, Yin deficiency, and Phlegm stasis had drug allergies or depression compared to those in subjects with none of the three constitutions (*P* < .05). The average overall HbA1C was 5.691% (SD=0.6674%). Higher proportions of subjects with Yin deficiency and Phlegm stasis had abnormal HDL levels (25.6% and 27.1%, respectively) than those in subjects without Yin deficiency and Phlegm stasis (*P* < .05) (Table 2).

Regarding personal health behaviors among the subjects with Yang deficiency, 77.7% did not smoke and 97.0% did not consume betel nuts. More than half of Yang deficiency subjects (62.9%), Yin deficiency subjects (63.1%), and Phlegm stasis subjects (66.0%) reported not exercising, with the highest proportion among the Phlegm stasis subjects. Regarding dietary characteristics, more than 60% of the Yang deficiency subjects and Yin deficiency subjects did not drink tea and a relatively high proportion (37.7%) of the Yang deficiency subjects drank coffee. Additionally, 35.4% of the Yin deficiency subjects and 38.8% of the Phlegm stasis subjects ate midnight snacks; these proportions differed significantly (*P* < .05) from those in subjects without Yin deficiency and subjects without Phlegm stasis (Table 3).

This study included a total of 403 (14.6%) patients with dry eyes. Table 4 presents the prevalence of dry eye for each constitution group. The prevalence of dry eye was significantly higher (*P* < .001) in the Yang deficiency (20.9%), Yin deficiency (25.3%), and Phlegm stasis subjects (23.9%) than in subjects without Yang deficiency (13.2%), Yin deficiency (12.0%), and Phlegm stasis (13.1%), respectively.

Table 5 shows the results of multiple logistic regression models, including an unadjusted model of the prevalence of dry eye regressed on the Yang deficiency, Yin deficiency, and Phlegm stasis as well as models adjusted for additional variables. The results showed that Yang deficiency, Yin deficiency, and Phlegm stasis subjects were more likely to develop dry eye than their counterpart groups without the corresponding deficiencies (crude odds ratio [OR]=1.741, 95% confidence interval [CI]=1.361–2.227; crude OR=2.4821, 95% CI=1.968–3.131; and crude OR=2.082, 95% CI=1.597–2.714, respectively). After adjusting for other risk factors, Yang deficiency, Yin deficiency, and Phlegm stasis showed strong significant correlations with dry eye (adjusted OR [AOR]=1.646, 95% CI=1.255–2.159; AOR=2.471, 95% CI=1.921–3.178; and AOR=2.224, 95% CI=1.657–2.986, respectively).

4. Discussion

This study is the first to investigate the association between common TCM constitutions including Yang deficiency, Yin deficiency, and Phlegm stasis and dry eye. After adjusting for demographic characteristics, chronic diseases, blood lipid levels, lifestyles, and other factors, including important risk factors such

Table 1
Relationship of TCM constitutions with demographic characteristics and chronic diseases (n=2760).

Characteristics	Yang deficiency		P	Yin deficiency		P	Phlegm stasis		P
	No n=2,253 (81.6)	Yes n=507 (18.4)		No n=2,218 (80.4)	Yes n=542 (19.6)		No n=2,384 (86.4)	Yes n=376 (13.6)	
	n (%)			n (%)			n (%)		
Age	49.34 ± 10.037	45.80 ± 9.723	<.001*	49.05 ± 10.044	47.20 ± 10.061	<.001*	49.26 ± 10.075	45.05 ± 9.268	<.001*
Sex			<.001			<.001			<.001
Male	1182 (52.5)	155 (30.6)		1137 (51.3)	200 (36.9)		1225 (51.4)	112 (29.8)	
Female	1071 (47.5)	352 (69.4)		1081 (48.7)	342 (63.1)		1159 (48.6)	264 (70.2)	
Marriage status			<.001			.102			<.001
Unmarried	364 (15.2)	120 (23.7)		376 (17.0)	108 (20.0)		394 (16.5)	90 (24.0)	
Married	1886 (83.8)	386 (76.3)		1839 (83.0)	433 (80.0)		1987 (83.5)	285 (76.0)	
Living alone			.072			.721			.601
No	2142 (95.1)	472 (93.1)		2099 (94.6)	515 (95.0)		2260 (94.8)	354 (94.1)	
Yes	111 (4.9)	35 (6.9)		119 (5.4)	27 (5.0)		124 (5.2)	22 (5.9)	
Education level			.681			.413			.175
Elementary and junior high	215 (9.5)	47 (9.3)		203 (9.2)	59 (10.9)		217 (9.1)	45 (12.0)	
Senior high (vocational)	695 (30.9)	147 (29.1)		675 (30.4)	167 (30.9)		726 (30.5)	116 (30.9)	
College or above [†]	1342 (59.6)	312 (61.7)		1339 (60.4)	315 (58.2)		1440 (60.4)	214 (57.1)	
Employment			.199			.995			.082
No	708 (31.5)	145 (28.6)		685 (31.0)	168 (31.0)		751 (31.6)	102 (27.1)	
Yes	1538 (68.5)	362 (71.4)		1526 (69.0)	374 (69.0)		1626 (68.4)	274 (72.9)	
BMI			.619			.773			.167
Normal	1118 (49.6)	261 (51.5)		1114 (50.2)	265 (48.9)		1206 (50.6)	173 (46.0)	
Excessive	803 (35.6)	179 (35.3)		782 (35.3)	200 (36.9)		843 (35.4)	139 (37.0)	
Obese	332 (14.7)	67 (13.2)		322 (14.5)	77 (14.2)		335 (14.1)	64 (17.0)	
Drug allergies			.003			.002			.011
No	2052 (91.1)	440 (86.8)		2022 (91.2)	470 (86.7)		2166 (90.9)	326 (86.7)	
Yes	201 (8.9)	67 (13.2)		196 (8.8)	72 (13.3)		218 (9.1)	50 (13.3)	
Chronic diseases			.259			.061			.299
Hyperlipidemia									
No	2008 (89.1)	443 (87.4)		1982 (89.4)	469 (86.5)		2123 (89.1)	328 (87.2)	
Yes	245 (10.9)	64 (12.6)		236 (10.6)	73 (13.5)		261 (10.9)	48 (12.8)	
Hypertension			.053			.775			.927
No	1906 (84.6)	446 (88.0)		1888 (85.1)	464 (85.6)		2031 (85.2)	321 (85.4)	
Yes	347 (15.4)	61 (12.0)		330 (14.9)	78 (14.4)		353 (14.8)	55 (14.6)	
Diabetes mellitus			.381			.853			.320
No	2129 (94.5)	484 (95.5)		2099 (94.6)	514 (94.8)		2253 (94.5)	360 (95.7)	
Yes	124 (5.5)	23 (4.5)		119 (5.4)	28 (5.2)		131 (5.5)	16 (4.3)	
Depression			<.001			<.001			<.001
No	2193 (97.3)	474 (93.5)		2158 (97.3)	509 (93.9)		2315 (97.1)	352 (93.6)	
Yes	60 (2.7)	33 (6.5)		60 (2.7)	33 (6.1)		69 (2.9)	24 (6.4)	

BMI=body mass index, TCM=traditional Chinese medicine.

*Independent *t* test.

[†] College or above, college or post-graduate education.

as depression and drug allergies, we observed that unbalanced constitutions were a risk factor for dry eye. Moreover, after correcting for the confounding effects of other factors, subjects with Yang deficiency, Yin deficiency, and Phlegm stasis were 1.6 to 2.5 times more likely to develop dry eye.

The most widely used instruments for classification of constitution types include, among others, the Constitution in Chinese Medicine Questionnaire (CCMQ), which was developed in Mainland China^[23] and the BCQ, which was developed in Taiwan.^[12–16] Although the mainland is very similar to Taiwan, the lifestyle and culture are different.^[18] This study adopted the BCQ scale for classification of constitution types.^[15] This questionnaire is easily administered and its reliability and validity have been established in quite a few studies.^[15,24–26] After adjusting for basic demographic characteristics and lifestyles, the results showed a correlation between TCM constitutions and dry

eye. TCM studies have shown that basic demographic characteristics such as sex, age, or education level are important factors affecting constitutions, with women, seniors, and those who have received high-level education more likely to develop unbalanced constitutions.^[11,27] In contrast, most Western medicine studies have indicated that basic demographic characteristics are risk factors for dry eye.^[7,28,29] Close relationships have been reported of old age, higher education, and dyslipidemia with the prevalence of dry eye, especially in women.^[28,30] The proportion of women with dry eyes is higher than that in men, which may be related to changes in hormones and tear secretion due to menopause. In addition, individuals with higher education levels have a higher chance of developing dry eyes because they are more likely to read or use computer, communication, and consumer (3C) products for long periods, especially in air-conditioned, dry environments. Compared to younger patients,

Table 2
Relationship between TCM constitutions and blood lipid levels (n=2760).

Characteristics	Yang deficiency		P	Yin deficiency		P	Phlegm stasis		P
	No n=2,253 (81.6)	Yes n=507 (18.4)		No n=2,218 (80.4)	Yes n=542 (19.6)		No n=2,384 (86.4)	Yes n=376 (13.6)	
	n (%)			n (%)			n (%)		
HbA1C			.554			.434			.546
Normal	1274 (56.5)	294 (58.0)		1252 (56.4)	316 (58.3)		1349 (56.6)	219 (58.2)	
Abnormal	979 (43.5)	213 (42.0)		966 (43.6)	226 (41.7)		1035 (43.4)	157 (41.8)	
TC			.114			.734			.625
Normal	1348 (59.8)	284 (56.0)		1315 (59.3)	317 (58.5)		1414 (59.3)	218 (58.0)	
Abnormal	905 (40.2)	223 (44.0)		903 (40.7)	225 (41.5)		970 (40.7)	158 (42.0)	
TG			.497			.928			.891
Normal	1810 (80.3)	414 (81.7)		1788 (80.6)	436 (80.4)		1922 (80.6)	302 (80.3)	
Abnormal	443 (19.7)	93 (18.3)		430 (19.4)	106 (19.6)		462 (19.4)	74 (19.7)	
HDL			.662			.021			.009
Normal	1762 (78.2)	392 (77.3)		1751 (78.9)	403 (74.4)		1880 (78.9)	274 (72.9)	
Abnormal	491 (21.8)	115 (22.7)		467 (21.1)	139 (25.6)		504 (21.1)	102 (27.1)	
LDL			.378			.333			.382
Normal	510 (22.6)	124 (24.5)		501 (22.6)	133 (24.5)		541 (22.7)	93 (24.7)	
Abnormal	1743 (77.4)	383 (75.5)		1717 (77.4)	409 (75.5)		1843 (77.3)	283 (75.3)	

Normal (HbA1C 4.6–6.4, TC < 200 mg/dL, TG < 150 mg/dL, LDL < 100 mg/dL, HDL > 40 mg/dL in men, and >50 mg/dL in women) or abnormal (HbA1c > 6.4, TC ≥ 200 mg/dL, TG ≥ 150 mg/dL, LDL ≥ 100 mg/dL, HDL ≤ 40 mg/dL in men, and ≥ 50 mg/dL in women).

HbA1C=glycosylated hemoglobin, HDL=high-density lipoprotein, LDL=low-density lipoprotein, TC=total cholesterol, TCM=traditional Chinese medicine, TG=total triacylglyceride.

Table 3
Relationship of different TCM constitutions with lifestyles (n=2760).

Characteristics	Yang deficiency		P	Yin deficiency		P	Phlegm stasis		P
	No n=2253 (81.6)	Yes n=507 (18.4)		No n=2218 (80.4)	Yes n=542 (19.6)		No n=2384 (86.4)	Yes n=376 (13.6)	
	n (%)			n (%)			n (%)		
Personal health behaviors									
Alcohol			.068			.115			.359
No	2060 (91.4)	476 (93.9)		2029 (91.5)	507 (93.5)		2186 (91.7)	350 (93.1)	
Yes	193 (8.6)	31 (6.1)		189 (8.5)	35 (6.5)		198 (8.3)	26 (6.9)	
Cigarette			.027			.664			.753
No	1643 (72.9)	394 (77.7)		1633 (73.6)	404 (74.5)		1757 (73.7)	280 (74.5)	
Yes	610 (27.1)	113 (22.3)		585 (26.4)	138 (25.5)		627 (26.3)	96 (25.5)	
Betel nut			.033			.512			.798
No	2136 (94.8)	492 (97.0)		2109 (95.1)	519 (95.8)		2269 (95.2)	359 (95.5)	
Yes	117 (5.2)	15 (3.0)		109 (4.9)	23 (4.2)		115 (4.8)	17 (4.5)	
Exercise			<.001			<.001			<.001
No	1190 (52.8)	319 (62.9)		1167 (52.6)	342 (63.1)		1261 (52.9)	248 (66.0)	
Yes	1063 (47.2)	188 (37.1)		1051 (47.4)	200 (36.9)		1123 (47.1)	128 (34.0)	
Dietary characteristics									
Tea			.014			.047			.076
No	1338 (59.4)	331 (65.3)		1321 (59.6)	348 (64.2)		1426 (59.8)	243 (64.6)	
Yes	915 (40.6)	176 (34.7)		897 (40.4)	194 (35.8)		958 (40.2)	133 (35.4)	
Coffee			.007			.059			.069
No	1561 (69.3)	320 (63.1)		1530 (69.0)	351 (64.8)		1640 (68.8)	241 (64.1)	
Yes	692 (30.7)	187 (36.9)		688 (31.0)	191 (35.2)		744 (31.2)	135 (35.9)	
Vegetarian			.209			.270			.169
No	2041 (90.6)	450 (88.8)		1995 (89.9)	496 (91.5)		2159 (90.6)	332 (88.3)	
Yes	212 (9.4)	57 (11.2)		223 (10.1)	46 (8.5)		225 (9.4)	44 (11.7)	
Midnight snacks			<.001			<.001			<.001
No	1646 (73.1)	316 (62.3)		1612 (72.7)	350 (64.6)		1732 (72.7)	230 (61.2)	
Yes	607 (26.9)	191 (37.7)		606 (27.3)	192 (35.4)		652 (27.3)	146 (38.8)	

TCM=traditional Chinese medicine.

Table 4
Relationship between TCM constitutions and dry eye.

Characteristics	Yang deficiency		P	Yin deficiency		P	Phlegm stasis		P
	No	Yes		No	Yes		No	Yes	
	n=2,253 (81.6)	n=507 (18.4)		n=2,218 (80.4)	n=542 (19.6)		n=2,384 (86.4)	n=376 (13.6)	
Dry eye			<.001			<.001			<.001
No	1956 (86.8)	401 (79.1)		1952 (88.0)	405 (74.7)		2071 (86.9)	286 (76.1)	
Yes	297 (13.2)	106 (20.9)		266 (12.0)	137 (25.3)		313 (13.1)	90 (23.9)	

TCM=traditional Chinese medicine.

older patients have poorer lacrimal gland secretory function and decreased neural regulation of lacrimal gland secretion. Older patients also have higher risks of meibomian gland dysfunction which often results in tear film instability.^[28] In the TCM theory, poor lifestyles can lead to unbalanced constitutions; for example, people who have a Phlegm stasis constitution are usually characterized by cigarette smoking, irregular sleep–wake rhythms, and fewer activities.^[31] Kawashima et al^[32] confirmed that good lifestyles can improve dry eye symptoms and promote the productivity and quality of life in dry eye patients. The results of the present study further revealed that, after adjusting for lifestyle factors, Yang deficiency, Yin deficiency, and Phlegm stasis were still significantly associated with dry eye.

Previous studies have confirmed that age, sex, use of contact lenses, and some chronic diseases including arthritis, allergies, thyroid disease, and migraine can contribute to the incidence of dry eye. Furthermore, the use of drugs such as antihistamines and steroids worsens dry eye.^[2,7,28,29] A Dana^[33] study revealed that the odds of developing dry eye in population with hypertension, thyroid disease, diabetes mellitus, sleep apnea, depression, and cardiovascular disease was 1.4 to 2.3 times that in the normal population; Um et al^[34] also reported that diabetes mellitus causes visual impairment, tear film instability, and ocular surface damage. Prolonged dry eye can lead to chronic pain, which can

result in depression and negatively impact life.^[35] The same study also revealed a higher prevalence of dry eye in depressed populations compared to that in populations without depression, which was attributed to the side effects of long-term antidepressant use.^[35] In this context, the present study also explored the association of risk factors such as chronic diseases, drug allergies, and depression with dry eye, and found that drug allergies, depression, Yang deficiency, Yin deficiency, and Phlegm stasis were all risk factors for dry eye, thus verifying the importance of constitutions in dry eye.

In the TCM theory, the concept of constitution covers human construction and physiological function.^[11] The TCM Yin–Yang notion emphasizes a dynamic balance between Yin and Yang to maintain a healthy physiological state. The Yin functions as “material” including organs and tissues, blood, body fluids, and nutrients, while the Yang functions as “energy” to regulate body organ function, ensure body fluid balance, and maintain temperature.^[36] Individuals with Yin–Yang imbalance but without a disease are deemed to fall in one of the two major categories of deficiency constitutions; namely, Yang deficiency or Yin deficiency.^[25] Individuals presenting with low physiological energy have constitutions with Yang deficiency; similarly, symptoms of insufficient body fluids indicate Yin deficiency.^[37] When the flow of Yin and Yang in the body are obstructed, the

Table 5
Multiple logistic regression of dry eye symptoms for TCM constitutions in different models.

Variables	Dry eye, OR (95%CI)								
	Yang deficiency			Yin deficiency			Phlegm stasis		
	AOR	95%CI	P	AOR	95%CI	P	AOR	95%CI	P
Model 1	1.741	(1.361–2.227)	<.001	2.482	(1.968–3.131)	<.001	2.082	(1.597–2.714)	<.001
Model 2	1.769	(1.359–2.304)	<.001	2.565	(2.006–3.280)	<.001	2.364	(1.774–3.150)	<.001
Model 3	1.730	(1.325–2.258)	<.001	2.532	(1.975–3.246)	<.001	2.325	(1.740–3.108)	<.001
Model 4	1.708	(1.307–2.233)	<.001	2.540	(1.979–3.260)	<.001	2.308	(1.724–3.089)	<.001
Model 5	1.683	(1.286–2.202)	<.001	2.507	(1.952–3.219)	<.001	2.262	(1.688–3.031)	<.001
Model 6	1.646	(1.256–2.157)	<.001	2.467	(1.919–3.171)	<.001	2.221	(1.656–2.979)	<.001
Model 7	1.646	(1.255–2.159)	<.001	2.471	(1.921–3.178)	<.001	2.224	(1.657–2.986)	<.001

AOR=adjusted odds ratio, CI=confidence interval, HbA1C=glycosylated hemoglobin, HDL=high-density lipoprotein, LDL=low-density lipoprotein, TC=total cholesterol, TCM=traditional Chinese medicine, TG=total triacylglyceride.

Body constitution: including Yang deficiency, Yin deficiency, and Phlegm stasis; Demographic characteristics: sex, age, education, employment, and BMI; Personal health behaviors: alcohol consumption, smoking, betel nut consumption, exercise habit; Dietary characteristics: tea, coffee, vegetarian food, midnight snacks; Lipid profile tests: HbA1C, TC, TG, HDL, and LDL; Chronic diseases: hyperlipidemia, hypertension, and diabetes mellitus.

Model 1: basic model.

Model 2: basic model plus adjusted for demographic characteristics.

Model 3: basic model plus adjusted for lifestyles (personal health behaviors and dietary characteristics).

Model 4: basic model plus adjusted for Lipid profile tests.

Model 5: basic model plus adjusted for Chronic diseases.

Model 6: basic model plus adjusted for depression.

Model 7: basic model plus adjusted for drug allergies.

constitution is referred to as Phlegm stasis.^[16] According to the theory of TCM constitutions, patients with Yin deficiency are prone to dry and hot skin due to lack of body fluids, thereby often manifesting dry cough with scanty phlegm and simultaneous lack of tears. Patients with Yang deficiency lack energy necessary for systemic circulation, so often present cold limbs and pale face. Moreover, patients with Yang deficiency often experience difficulty in fully closing one's eyes during sleep, which may explain why tears are prone to evaporation and thus inadequate. Patients with Phlegm stasis have poor blood circulation in the body, which is not conducive to metabolism. Therefore, patients often experience problems such as obesity and high sebum secretion. These patients may have abnormal lipid secretion and metabolism in the meibomian glands, which indirectly destabilizes the lipid layer of tears, causing the tears to readily evaporate, resulting in dry eye.^[6] However, these inferences regarding the relationships of Yang deficiency, Yin deficiency, and Phlegm stasis to dry eye require further investigation.

Western medicine administers different treatments for dry eye according to the symptom severity. These treatments include the use of goggles to maintain periocular humidity, frequent application of hot moist compresses around the eye, enhanced cleaning of the eyelid margin, avoidance of medications that worsen dry eye, and supplementation with artificial tear.^[6] However, the current widely used commercial artificial tears mostly contain preservatives; thus, their long-term use may damage corneal epithelial cells.^[38] The steroid eyedrops commonly used in dry eye treatments may cause side effects with long-term use such as cataract formation, increased intraocular pressure (IOP), and increased risk of ocular infections.^[38] In recent years, a growing number of dry eye patients have resorted to TCM after failing to obtain satisfactory outcomes from Western medical treatments. One study revealed that nearly one in five dry eye patients were unsatisfied with treatment outcomes.^[7] At present, TCM is considered a complementary and alternative medicine.^[8] The TCM theory states that individuals are unique; thus, the overall physical condition should be addressed with a focus on patient individuality, especially their disease susceptibility, to provide individuals with corresponding treatment and prevention measures to promote health management.^[17,39] In TCM, different constitutions are treated with different Chinese herbal medicines whose composition and doses are adjusted according to individual clinical manifestation. For example, the most obvious manifestation of Yang deficiency are feelings of cold and less subcutaneous fat; Yin deficiency patients often feel thirsty and present with dry eye, hot flush, constipation, low urine volume, fast heart rate, and insomnia^[17,40,41]; Phlegm stasis patients are prone to obesity, diabetes mellitus, or other metabolic diseases.^[31,34] Other treatments include wolfberry, an anti-inflammatory and antimicrobial substance, as well as curcumin, which contains natural antioxidants, can also alleviate dry eye symptoms.^[9,10] In a meta-analysis study of six randomized controlled trials, treatment of dry eye patients with acupuncture significantly improved tear break-up time, Schirmer test scores, and the extent of cornea fluorescein staining.^[42] The moxibustion in TCM is similar to application of hot moist compresses in Western medicine, as the generated heat in moxibustion can also effectively improve dry eye symptoms.^[43]

The TCM constitution theory reflects an individual's current health status and future health trends from four aspects; namely, physiological differences, life processes, psychological condi-

tions, and adaptability to natural and social environments. Studies have confirmed that Yang deficiency, Yin deficiency, Phlegm stasis and lifestyles are highly correlated to dry eye. To manage a disease, the focus will shift from reactive approach to proactive approach in the future. As patients with dry eye are not fully satisfied with current treatment options, the integration of TCM and Western medicine may serve as an alternative treatment option. Individualized lifestyle recommendations and treatments should be provided to patients with different TCM constitutions to improve or effectively alleviate dry eye symptoms.

4.1. Study limitations

In our study, we explore the relationship between a single body constitution and dry eye. The relationship between the mixed body constitution and dry eye should be investigated further. Second, since this study was based on the TWB database, it was not possible to conduct the study prospectively. However, we recognize the importance of a prospective study to validate the findings here, and will include a prospective design in future studies in multi-layered approaches. Despite these limitations and the less rigorous research hypotheses, the results support the correlation and impact of different TCM constitutions on dry eye.

5. Conclusions

Subjects with one of Yang deficiency, Yin deficiency, and Phlegm stasis were prone to dry eye. In the future, different prevention recommendations and disease treatments can be provided from the perspective of preventive medicine for patients with different constitutions to alleviate the impact of dry eye. The combination of healthy lifestyles with different TCM and Western medicine treatments is recommended to reduce the vicious cycle of the disease and alleviate the discomfort of dry eye.

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