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1 **The Eye-image Features of Patients with Coronary Heart Disease**

2 **Assesed:A prospective, observational study of traditional Chinese**

3 **medicine combined with modern medicine**

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14

15 **Abbreviation:**

16 AI, artificial intelligence, CAG, Coronary angiography; CABG, coronary artery

17 bypass grafting; CHD, coronary heart disease; Cr, creatinine, EF, ejection fraction;

18 HbA1C, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density

19 lipoprotein; TCM, traditional Chinese medicine; PCI, percutaneous coronary

20 intervention; PVD, peripheral vascular disease; T-Ch, total cholesterol; TG, total

21 triglyceride.

22 **Abstract**

23 **BACKGROUND:** Coronary heart disease (CHD) significantly impacts human health.

24 Traditional Chinese medicine (TCM) suggests a possible correlation between eye-

25 image and CHD, but this relationship has not been fully explored in Western

26 medicine.

27 **PURPOSE:** We aim to investigate the potential causal relationship between eye-  
28 image features and CHD, as examined by coronary angiography (CAG).

29 **METHODS:** The study selected patients hospitalized in the Department of  
30 Cardiology from November 15, 2021, to February 27, 2022. The selected patients  
31 were divided into two groups based on their CAG findings: the CHD group (at least  
32 one coronary lesion stenosis $\geq$  50%) and the control group (lesion stenosis $<$ 50%)

33 **RESURTS:** The final analysis included 342 patients out of a total of 426 participants,  
34 of these, 165 patients (48.2%) were diagnosed with CHD. The study found that  
35 certain characteristics in the left region 5(L5) and right region ( R5) were associated  
36 with CHD, including L5 pink dark speckle (OR: 4.143, 95%CI: 1.135-15.124,  
37  $P=0.031$ ), L5 vascular tortuosity (OR: 0.234, 95%CI: 0.077- 0.71,  $P=0.010$ ) R5 dark  
38 red blood vessels (known as Xue mai in TCM) (OR: 1.683, 95%CI: 1.035-2.738,  
39  $P=0.036$ ), and R5 yellowish mounds (OR: 2.083, 95%CI: 1.221-3.554,  $P= 0.007$ ).  
40 Multivariate regression analyses showed that L5 vascular tortuosity had a negative  
41 correlation with CHD.

42 **CONCLUSION:** Our study revealed that four types of eye-image features, namely  
43 pink dark speckle, vascular tortuosity, dark red blood vessels, and yellowish mounds  
44 are associated with CHD. Among these features, vascular tortuosity showed a  
45 negative correlation with CHD, which could potentially aid in the diagnosis of the  
46 disease.

47 **Key words:** Eye-image; Coronary heart disease; Traditional Chinese medicine

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49

## 50 **Introduction:**

51 Coronary heart disease (CHD) is mainly caused by coronary atherosclerotic  
52 plaque or coronary artery spasm, leading to coronary artery stenosis, blood supply  
53 restriction, and myocardial ischemia and hypoxia<sup>[1]</sup>. Many studies have confirmed that  
54 CHD is the leading cause of cardiovascular death and chronic disability worldwide<sup>[2]</sup>,  
55 becoming one of the health-threatening problems<sup>[3]</sup>. According to the World Health  
56 Organization, traditional Chinese medicine (TCM) is considered a branch of Western  
57 medicine that is used as an alternative or complementary treatment option  
58 worldwide<sup>[4]</sup>, TCM is widely used in the daily lives of many Asians <sup>[5, 6]</sup>, and has  
59 accumulated rich clinical experience<sup>[7]</sup>. Furthermore, TCM eye-image examination  
60 has the potential to be a valuable diagnostic tool for coronary heart disease (CHD) <sup>[8]</sup>.  
61 Previous studies have identified several eye-image features in the heart-eye region  
62 that are related to CHD according to TCM principles<sup>[9]</sup>. However, controversy exists  
63 due to differences in subjective or empirical factors among physicians and the lack of  
64 randomized, double-blind, placebo, and controlled clinical trials <sup>[10]</sup>.

65 TCM believes that different parts of the sclera reflect the condition of different  
66 viscera. The color of speckles, mounds, and fogs in the eyes, as well as the color of  
67 blood vessels (called *Xue mai* in TCM) in the responding organ, can reflect the health  
68 of internal organs such as the lungs, kidneys, or heart <sup>[11]</sup>. According to the theory of  
69 TCM, 15 regions of each eye correspond to different 15 organs of the body.  
70 Particularly, the Left region 5 (L5) and Right region 5(R5) are believed to be related  
71 to the condition of the heart. These regions are located near the canthus of the eye,  
72 while the other side is closer to the pupil, as shown in **Figure 1**.

73 Coronary angiography (CAG) is currently considered the most reliable method  
74 of diagnosing CHD <sup>[12]</sup>. However, it is an invasive and expensive procedure<sup>[13]</sup>. And  
75 traditional biomarker discoveries are not sufficient to provide a deeper understanding  
76 of the mechanisms implicated in CHD <sup>[14]</sup>. Therefore, in this study, a low-cost, simple,  
77 and novel method was used to evaluate CHD using eye-image features of integrated  
78 TCM and Western medicine.

## 79 **Methods**

80 This paper was a single-center, retrospective, observational study consisting of  
81 426 participants who were admitted to the Department of Cardiology at the Second  
82 Affiliated Hospital of Harbin Medical University (Harbin, China) between November  
83 15, 2021, and February 27, 2022. The inclusion criteria for the study were patients  
84 aged 18-85 who were suspected of having CHD and were undergoing a CAG  
85 examination. Patients with a history of eye disease or surgery, such as infection,  
86 glaucoma, cataract, and so on, were excluded from the study. In addition, patients who  
87 wear colored contact lenses or artificial eyes are also excluded, Patients with PCI,  
88 CABG history as well as heart valve defects, and congenital heart defects are also  
89 excluded, as well as those whose eye-image pictures cannot be analyzed. Selected  
90 patients were divided into two groups according to angiographic stenosis<sup>[13]</sup>: the CHD  
91 group (at least one coronary artery stenosis of  $\geq 50\%$ ), and the Control group (lesion  
92 stenosis  $< 50\%$ ). A total of 342 eligible patients provided informed consent and  
93 participated in the research, undergoing both CAG and eye-imaging testing. The  
94 detailed study flowchart is illustrated in **Figure 2**.

### 95 **CAG examination**

96 All selected patients were blinded to relevant studies via the femoral or radial  
97 artery by experienced interventional physicians. Using more than two orthogonal  
98 projection points to identify each lesion, stenosis grade was expressed as a percentage  
99 of coronary stenosis diameter and grouped according to coronary stenosis grade score.

### 100 **Eye-image system examination**

101 The Capital Bio MyEyeD-10 system was utilized to examine eyes which  
102 combines the principles of both Chinese and Western medicine using advanced optical  
103 technology and artificial intelligence (AI). The system was additionally improved  
104 with the integration of the Askya imaging system, which has an impressive resolution  
105 of 28 million pixels.

106 The well-trained physician instructed the patient to place their eye on the small  
107 hole of the machine as shown in **Figure 3A**. Then the physician guided the patient to

108 lift or pull down their eyelids with their finger to fully expose the sclera and rotate the  
109 direction of the eyeball. Once the light hit the sclera on the opposite side of the iris,  
110 the doctor quickly captured an image of the eye into the computer imaging system,  
111 this process was repeated for the other eye. Finally, eye-image were captured from  
112 five different angles (superior, inferior, left, right, and frontal) of each eye, as  
113 illustrated in **Figure 3B**, the analysis of the R5 and L5 regions was then collected.

114 The eye-image system can automatically identify the color, shape, and size of the  
115 eye-image characteristics of patients with CHD. This is done by analyzing abnormal  
116 pathological phenomena in the heart-eye area, as well as determining whether the  
117 features protrude from the surface of the sclera. Based on these characteristics, the  
118 system can automatically name and judge the types of TCM syndromes that the  
119 patient may be experiencing. For example, speckles do not protrude from the surface  
120 of the sclera and are round, oval, or variously irregular in shape, and the pink dark  
121 speckle indicates blood stasis and blood deficiency. Mounds are round, oval, or  
122 irregular opaque bulges, with a diameter greater than 2mm, which is higher than the  
123 surface of the white eyes, and yellowish mounds are attributed to damp phlegm and  
124 blood stasis. Diseased blood vessels are no-red vessels of different lengths on the  
125 sclera, and dark red vessels are primarily caused by blood stasis. Vascular tortuosity is  
126 characterized by the repeated twisting and turning of blood vessels, regardless of  
127 color, and can display a continuous or intermittent state of contraction. This condition  
128 is primarily associated with Qi stagnation and blood stasis<sup>[15]</sup>. Pictures of eye-features  
129 as shown in **Figure 4**.

### 130 **Baseline data collection**

131 To collect comprehensive medical history, information regarding diabetes,  
132 hypertension, stroke, and peripheral vascular disease (PVD) history. Additionally, it is  
133 important to obtain lifestyle habits including smoking history, including both past and  
134 present conditions. This should be accompanied by auxiliary examination results and  
135 laboratory values, such as ejection fraction (EF), glycated hemoglobin (HbA1c),  
136 creatinine (Cr), total cholesterol (T-Ch), total cholesterol (TG), HDL protein (HDL),

137 low-density lipoprotein (LDL), and other relevant data.

## 138 **Statistical analysis**

139 Statistical analysis was performed using SPSS V.25.0, continuous variables were  
140 presented as mean  $\pm$  standard deviation, while categorical variables were presented as  
141 percentages. We also employed the chi-square test to compare categorical variables  
142 and the t-test to compare continuous variables. Additionally, we calculated exact 95%  
143 confidence intervals (CI) for all diagnostic performances. Univariate regression  
144 analysis and categorical variables were used to the comparison of the eye-image  
145 features in the CHD group and control group, and to analyze eye-image features using  
146 multivariate regression. In this study,  $P$ -values  $<0.05$  was considered statistically  
147 significant.

## 148 **Results**

149 From November 15, 2021, to February 27, 2022, a total of 426 patients  
150 underwent CAG and eye-image system examinations, 84 patients (19.7%) who did  
151 not meet the inclusion criteria were excluded, and 342 patients were included in the  
152 final analysis. Of all participants, 165 (48.2%) were diagnosed with CHD, of whom  
153 116 (70.3%) were male, with a mean age of  $58.7 \pm 7.6$  years. Additionally, 93 (56.4%)  
154 had hypertension, 66 (40.0%) smoked, and 38 (23.0%) had diabetes, and there were  
155 fewer cases of strokes and PVD (**Table 1**).

156 In the study on eye-image features, we identified a total of 39 distinct features,  
157 including macula around the black eye, vascular tortuosity, and 6 colors of blood  
158 vessels,  
159 as well as various colors and shapes of speckles, mounds, spots, fogs, and Yue yuns.  
160 We further categorized these features into 8 colors of speckles, 7 colors of mounds, 6  
161 colors of spots and fogs, and 4 colors of *Yue yuns* as shown in **Table 2**. An atypical  
162 colorless eye-image feature picture is shown in **Figure 4**. This study identifies 14  
163 colors associated with CHD that appear in various forms and blood vessels. These  
164 colors include pink dark, dark pink, pink red, pink, dark red, red dark, red, yellow,  
165 dark yellow, pink yellow, pastel yellow, light yellow, and tan, as well as various light



166 and grey. Our research indicates that colors associated with CHD are primarily  
167 compound colors, such as dark red and pink dark, as well as light yellow.  
168 Interestingly, among single colors, red was found to be associated with the control  
169 group. We found that the four eye-image features related to CHD are all related to  
170 blood stasis, among them, the pink dark speckle, yellowish mound, and dark red  
171 blood vessel are positively correlated with CHD, while the tortuous blood vessel is  
172 negatively correlated with CHD.

173 After analyzing all the eye-image using the Capital Bio MyEyeD-10 system, we  
174 compared the differences in eye-image features between two groups of patients as  
175 shown in [Table 2](#). Interestingly, we discovered that 5 eye-image features were  
176 significantly different between the two groups, as shown in [Figure 5](#). There are L5  
177 pink dark speckles (6.7% vs 1.7%,  $P=0.020$ ), R5 dark red blood vessels (31.5% vs  
178 21.5%,  $P=0.035$ ), and R5 yellowish mound (27.3% vs 15.3%,  $P=0.006$ ) and L5  
179 vascular tortuosity (2.4% vs 9.6%,  $P=0.006$ ) associated with CHD, and the R5 red  
180 blood vessel (0.0% vs 5.6%,  $P=0.005$ ) is related with the control group.

181 The Univariate regression analysis results of eye-image features showed that  
182 there was a significant correlation between the 4 types of eye-image features and  
183 CHD, including L5 pink dark speckle (OR: 4.143, 95%CI: 1.135-15.124,  $P=0.031$ ),  
184 L5 vascular tortuosity (OR: 0.234, 95%CI: 0.077-0.71,  $P=0.010$ ), R5 dark red blood  
185 vessel (OR: 1.683, 95%CI: 1.035-2.738,  $P=0.036$ ), and R5 yellowish mound (OR:  
186 2.083, 95% CI: 1.221 - 3.554,  $P=0.007$ ), as shown in [Table 3](#). In multivariate  
187 regression analysis was conducted to investigate the association between vascular  
188 tortuosity and CHD, while controlling for variables with statistical significance in a  
189 single factor and excluding the influence of collinearity. After adjusting for gender,  
190 age, smoking, and serum glucose, the results revealed that vascular tortuosity  
191 remained negatively associated with CHD. ([Table 4](#))

## 192 Discussion

### 193 Examination New Observation of CHD Patients

194 In this single-center, retrospective, and observational study, we identified



195 significant differences in eye-image features between individuals with CHD and those  
196 without. Our analysis revealed four distinct eye-image features representing blood  
197 stasis associated with CHD, namely pink dark speckle, vascular tortuosity, dark red  
198 blood vessels, and yellowish mounds. Prior research indicates that a healthy person's  
199 sclera is smooth and glossy, resembling the appearance of egg white, with no visible  
200 blood vessels. However, the onset of certain illnesses can alter this appearance, the  
201 sclera becomes abnormal, regardless of the severity of the disease or whether the body  
202 shows any symptoms<sup>[9, 11]</sup>, and significant changes occur in the corresponding organ-  
203 eye region<sup>[4, 11]</sup>. As the disease progresses, eye-image features form in connection with  
204 the ophthalmic veins or arteries on the surface or deep layer of the sclera<sup>[9]</sup>. In TCM,  
205 Yin-Yang and five-element theory mean the eye link to the heart<sup>[16]</sup> and other organs,  
206 also suggesting that the eyes are not an independent entity but are related to the  
207 human body's internal environment<sup>[17]</sup>. Utilizing a non-invasive technique to extract  
208 eye-image characteristics from the heart-eye region can effectively diagnose the  
209 presence of CHD in a patient. This method is both cost-effective and straightforward  
210 and does not necessitate a specialized environment.

211 We demonstrated the validity of the TCM eye-image of CHD, which recognizes  
212 the human body as a unified whole<sup>[16]</sup> with interconnected organs and external  
213 manifestations of internal changes. For example, research has demonstrated that  
214 kidney disease can cause the thickening of the blood vessels in the kidney-eye area on  
215 the sclera, sometimes exceeding 0.24mm<sup>[11]</sup>. Our study conclusion shows a correlation  
216 between the eye-image features of the heart-eye area and CHD, which aligns with the  
217 holistic concept of TCM. Another important aspect is syndrome differentiation and  
218 treatment, as only accurate differentiation can lead to effective treatment. In TCM,  
219 CHD is diagnosed through patient *Zheng hou* (known as symptoms in Western  
220 medicine), which include cold and heat, deficiency and excess, phlegm dampness, and  
221 stasis<sup>[1, 18]</sup>. The disease *Zheng hou* of patients with CHD can be determined by  
222 analyzing the eye-image characteristics of the heart-eye area. This information can  
223 guide clinicians to choose appropriate treatment options using traditional Chinese or

224 Western medicine.

### 225 **Eye-image features related to CHD**

226 The four types of eye-image features related to CHD are all closely related to  
227 blood stasis, the source of blood stasis may be related to trauma, Qi and blood  
228 disorders, and pathogenic cold and heat[14]. Studies have shown that there is a certain  
229 correlation between blood stasis and the complexity of CHD, and the severity of  
230 blood stasis is an important factor for restenosis after percutaneous coronary  
231 intervention. It can be seen that blood stasis is closely related to patients with CHD<sup>[19]</sup>.  
232 Epidemiological studies in recent years have shown that stasis is the main syndrome  
233 of CHD, among 5284 patients with CHD, blood stasis accounted for 79.3%<sup>[7]</sup>, In our  
234 study on eye-image features and their relation to CHD, yellowish mounds were the  
235 most commonly associated feature in Western medicine. These mounds are typically  
236 attributed to damp phlegm and blood stasis, as found in previous research<sup>[1, 18]</sup>.  
237 According to research<sup>[14]</sup>, this condition is exacerbated by consuming large amounts  
238 of high-fat food and a lack of exercise, leading to the accumulation of lipids,  
239 increased blood lipid and blood cell adhesion, and the development of blood stasis<sup>[1]</sup>.  
240 It can be seen that the pathological process of blood stasis is consistent with the  
241 reason CHD is interlinked between Chinese and Western medicine<sup>[1, 14]</sup>.

### 242 **Zheng hou and Eye-image features related to CHD**

243 The research indicates that changes in the blood vessels of the eyes can evaluate  
244 the degree of microvascular and coronary lesions and also assess cardiovascular  
245 disease<sup>[20]</sup>, to some extent, retinal vascular changes can also predict cardiovascular  
246 events<sup>[17]</sup>. The iris theory also supports that CHD is related to the eyes<sup>[21]</sup>, by  
247 identifying the irregularity of the iris pigment between 2-3 points (roughly in the  
248 heart-eye area), it can be determined whether there is a lesion in the heart. Recently,  
249 applying a deep learning algorithm to analyze the eyes to develop CHD models to  
250 predict many cardiovascular risk factors and *Zheng hou* in TCM<sup>[22]</sup>, with the help of  
251 AI and the combination of traditional Chinese<sup>[23]</sup> and Western medicine<sup>[24]</sup>, the  
252 potential reason between TCM of AI<sup>[25]</sup> will become more and more clear in the

253 future. Eye image features are inseparable from blood vessels, which can be seen on  
254 the sclera and connected to blood vessels deep in the sclera that cannot be seen with  
255 the naked eye<sup>[9]</sup>. Eye-image features may indicate panvascular disease or an  
256 extension of ocular atherosclerosis, but further research is needed to confirm these  
257 findings.

258 This study introduces a novel idea – that the vascular tortuosity on the heart-eye  
259 region of the sclera is negatively correlated with CHD. Previous research has  
260 established a negative correlation between retinal artery stenosis and CHD<sup>[26]</sup>. If we  
261 can confirm that the tortuous vascular structure is an artery and obtain precise  
262 measurements, we may be able to obtain more comprehensive and meaningful results.  
263 If it is confirmed that the tortuous blood vessels on the surface of the sclera are  
264 negatively correlated with coronary heart disease, it is more concise and convenient  
265 than detecting retinal arteries in the fundus.

266 Several studies have reported different levels of corneal changes in patients with  
267 CHD<sup>[26-28]</sup>. However, CHD is not only associated with the cornea but also with the  
268 sclera and retina of the eye. All three structures may contain similar markers that  
269 could help explain the link between CHD and the eyes. In this study, we found that  
270 the eye-image features of CHD patients were related to their left and right eyes,  
271 respectively. Chinese and Western medicine support research on the relationship  
272 between the left eye and the heart<sup>[9, 20]</sup>, indicating that more research is needed.

### 273 **Limitations**

274 The study has a small sample size and is limited to a single-center experiment.  
275 Future studies should include multicenter participation to avoid any deviations in the  
276 collection of eye-image features and data processing. Additionally, the study only  
277 collected static eye-images and did not consider dynamic attributes.

### 278 **Conclusion**

279 Our study discovered distinct eye-image features in individuals with CHD, as  
280 compared to the control group. We propose a simple and feasible method that can aid  
281 in the screening of CHD during community physical examinations. If a patient

282 exhibits typical eye image features, it may suggest a higher probability of CHD, and  
283 further examination is recommended.

284 .

#### 285 **Authors contribution**

286 Zhanqun Gao and Dirui Zhang: Conceptualization, Validation, Writing, Data  
287 analysis and statistical processing: Luping He, Yishuo Xu, Validation, Investigation, Writing:  
288 Ziqian Weng and Shengfang Wang, Data analysis: Boling Yi and Zhi Zhang, Data  
289 collection: Yubo Gao and Wei Hao, Data collection, Writing – original draft: Chunqi Xie,  
290 Yuhan Qin, Writing – review & editing: Ming Zeng, Xue Feng, Minghao Liu, and Chen  
291 Zhao: Draft revision, Haibo Jia and Chao Fang: Manuscript review and editing. Sining  
292 Hu and Bo Yu designed the whole experiment. All authors agree to accept full  
293 responsibility for all aspects of their work and to ensure completeness and accuracy.

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#### 297 **Conflict of interest**

298 We declare that there are no conflicts of interest in the publication and content of  
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300

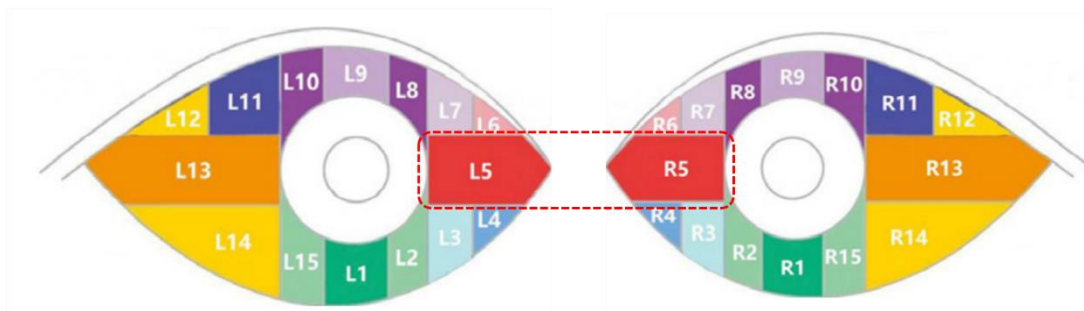
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395 **Figure 1** Schematic diagram of the relationship between the sclera and viscera

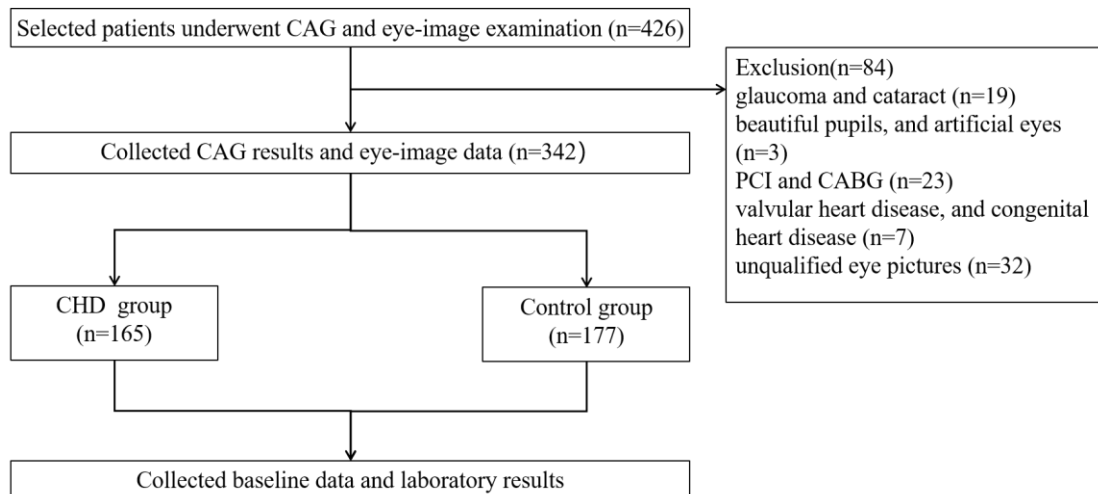
396 L-left eye, R-right eye, 1, stomach; 2,15 spleen; 3, large intestine; 4, small intestine;

397 5, heart; 6, breast; 7, lung; 8, 10, kidney; 9, bladder; 11, reproductive system; 12, 14,

398 liver; 13, gallbladder

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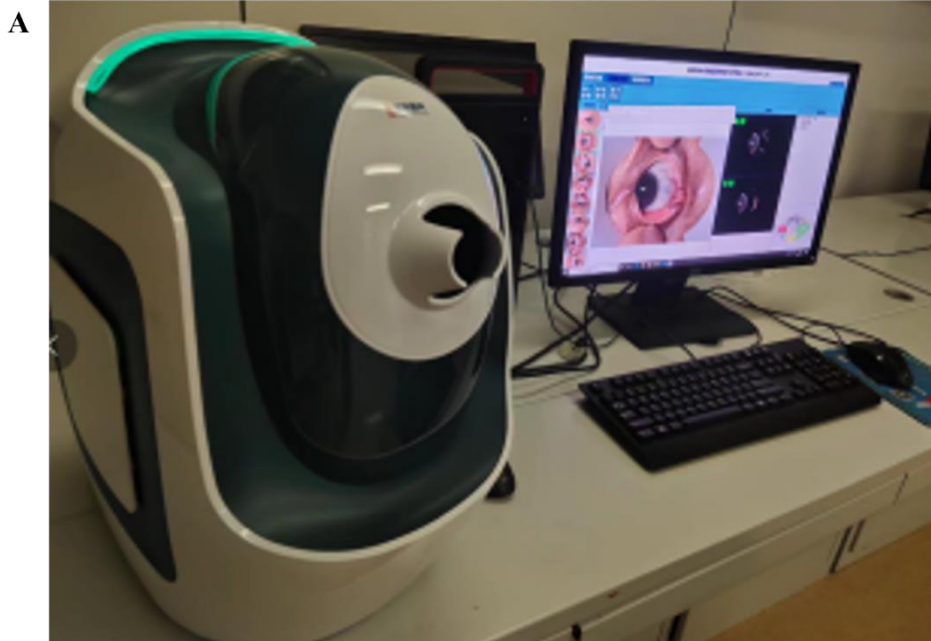
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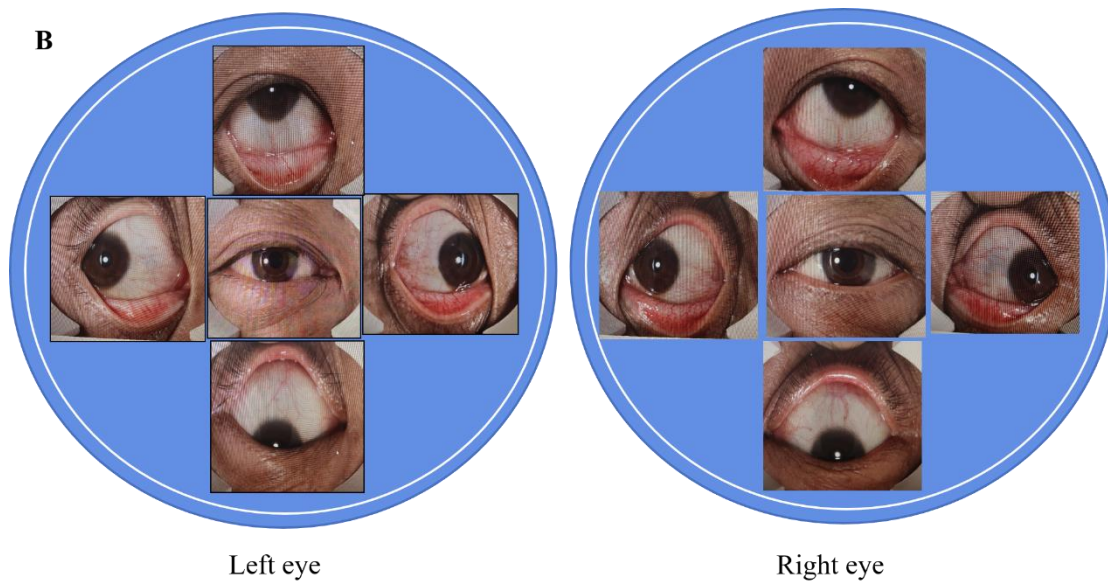
**Figure 2** Study flowchart

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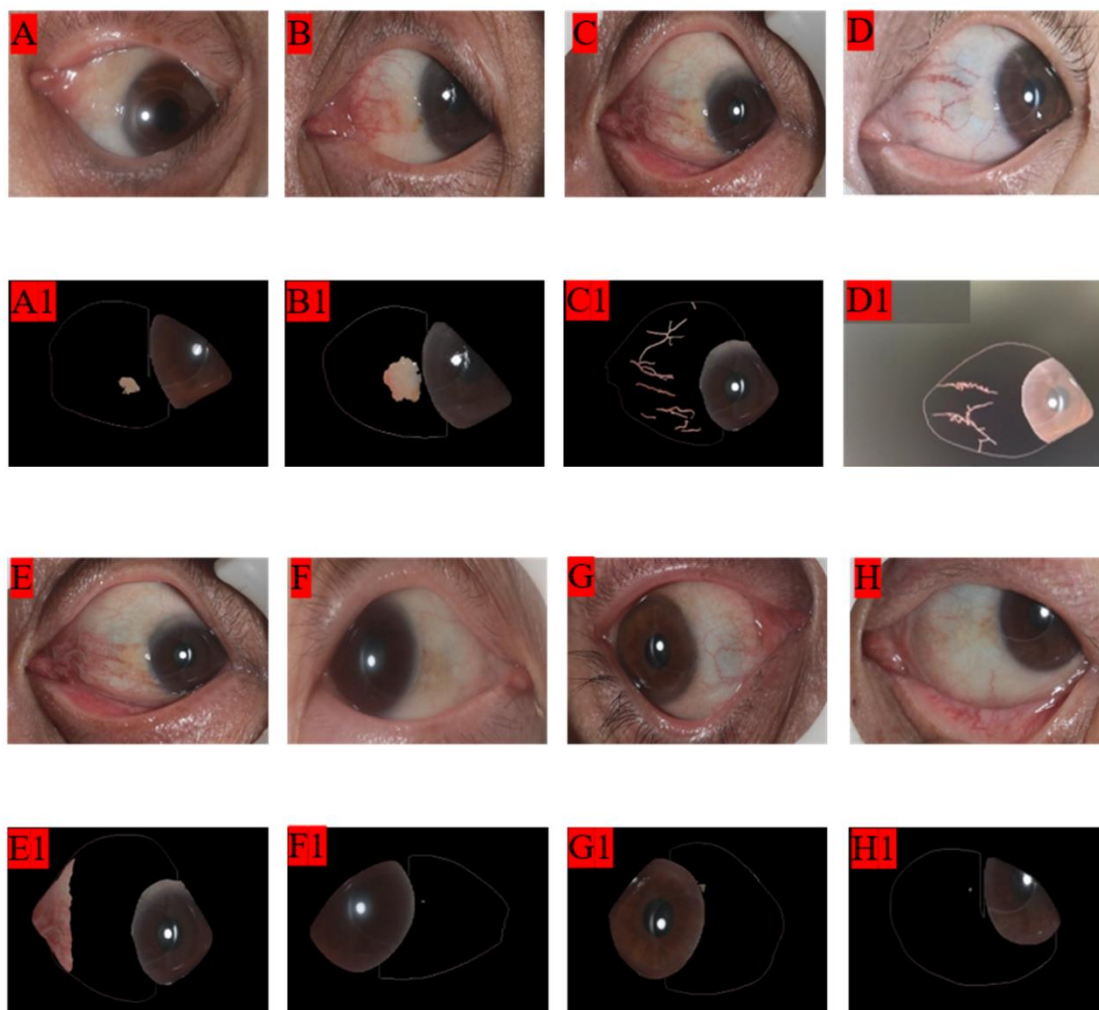
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**Figure 3** The eye-image system and taken pictures.

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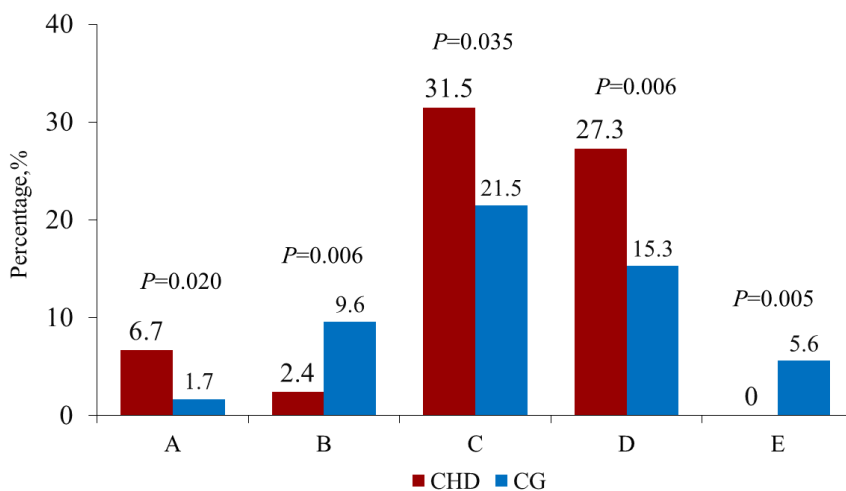
418 **Figure 4** Eye-image forms and blood vessel  
419 A-H shows the taken eye-image pictures. A1-H1 shows analyzed eye-image  
420 forms in the eye-image system. A, A1, speckle, B, B1, mound, C, C1, blood  
421 vessel, D, D1, vascular tortuosity, E, E1, fog, F, F1, spot, G, G1, macula around  
422 black eye, H, H1, *Yue yun*  
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**Figure 5** Meaningful eye-image features in the CHD group and CG(control group)

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A, pink dark speckle; B, L5 vascular tortuosity; C, R5 dark red blood vessel; D, R5

430

yellowish mound; E, R5 red blood vessel

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435

436 **Table 1**

437 **Comparison of general data between the CHD group and the control group**

	Total(n=342)	CHD (n=165)	CG (n=177)	<i>P</i> value
Male, n (%)	192 (56.1)	116 (70.3)	76 (42.9)	< 0.001
Age, year	57.8±8.7	58.7±7.6	56.9±9.5	< 0.001
Diabetes, n (%)	60 (17.5)	38 (23.0)	22 (12.4)	0.010
Hypertension, n (%)	167 (48.8)	93 (56.4)	74 (41.8)	0.007
PVD, %	11 (3.2)	4 (2.4)	7 (4.0)	0.423
Stroke, n (%)	30 (8.8)	19 (11.5)	11 (6.2)	0.083
Smoking, n (%)	98 (28.7)	66 (40.0)	32 (18.1)	< 0.001
Serum glucose, mmol/	6.0±1.9	6.4±2.4	5.6±1.3	0.001
HbA1c, %	6.0±1.1	6.4±1.3	5.8±0.7	0.001
Cr, umol/l	70.9±35.8	72.9±30.7	69.1±39.8	0.322
TG, mmol/L	1.8±1.0	1.8±1.0	1.7±1.0	0.347
HDL, mmol/L	1.1±0.3	1.1±0.3	1.2±0.3	< 0.001
LDL, mmol/L	2.9±0.9	3.0±1.0	2.8±0.8	0.283
T-Ch, mmol/L	4.4±1.0	4.4±1.1	4.5±0.93	0.672
LVEF, %	62.3±4.6	61.7±5.0	62.9±4.2	0.025

438 Values are mean SD, n (%), or mean (range). *p* values were determined by using an analysis of  
 439 variance with a Bonferroni post hoc method for continuous variables and Fisher exact test for  
 440 categorical variables.

441 **Table 2**

442 Comparison of the eye-image features in the CHD group and control group

Eye-image features	L5		<i>P-value</i>	R5		<i>P-value</i>
	CHD (n=165)	CG (n=177)		CHD (n=165)	CG (n=177)	
<b>Macula around black eye</b>	42 (25.5)	31 (17.5)	0.073	38 (23.0)	29 (16.4)	0.122
<b>Speckle</b>						
Pink dark	11 (6.7)	3 (1.7)	0.020	3 (1.8)	2 (1.1)	0.937
Red dark	5 (3.0)	3 (1.7)	0.647	8 (4.8)	14 (7.9)	0.249
Yellow	12 (7.3)	15 (8.5)	0.68	3 (1.8)	3 (1.7)	1.000
Dark yellow	9 (5.5)	7 (4.0)	0.512	9 (5.5)	6 (3.4)	0.351
Light	0(0)	5 (2.8)	0.085	6 (3.6)	2 (1.1)	0.24
Grey	3 (1.8)	0(0)	0.222	2 (1.2)	0(0)	0.448
Red	0(0)	1 (0.6)	0.334	2 (1.2)	1 (0.6)	0.951
Pink-red	1 (0.6)	1 (0.6)	1.000	0(0)	0(0)	1.000
<b>Spot</b>						
Pink dark	6 (3.6)	5 (2.8)	0.671	2 (1.2)	3 (1.7)	1.000
Red dark	4 (2.4)	2 (1.1)	0.618	6 (3.6)	4 (2.3)	0.664
Dark yellow	8 (4.8)	4 (2.3)	0.194	1 (0.6)	2 (1.1)	1.000
Grey	2 (1.2)	2 (1.1)	1.000	3 (1.8)	2 (1.1)	0.937
Light	2 (1.9)	2 (1.1)	1.000	0(0)	3 (1.7)	0.272
Red	0(0)	1 (0.6)	1.000	0(0)	0(0)	1.000
<b>Mound</b>						
Yellowish	45 (27.3)	34 (19.2)	0.077	45 (27.3)	27 (15.3)	0.006
Light	29 (17.6)	31 (17.5)	0.988	13 (7.9)	11 (6.2)	0.547
Dark yellow	14 (8.5)	16 (9.0)	0.856	6 (3.6)	4 (2.3)	0.45
Grey	1 (0.6)	2 (1.1)	1.000	5 (3.0)	7 (4.0)	0.642
Pink yellow	2 (1.2)	5 (2.8)	0.503	2 (1.2)	4 (2.3)	0.461
Pink	3 (1.8)	2 (1.1)	0.937	30 (18.2)	35 (19.8)	0.708
Dark red	1 (0.6)	1 (0.6)	1.000	1 (0.6)	0(0)	0.972

443

Eye-image features	L5		<i>P-value</i>	R5		<i>P-value</i>
	CHD	CG		CHD	CG	
<b>Blood vessel</b>						
Pink dark	74 (44.8)	71 (40.1)	0.376	54 (32.7)	62 (35.0)	0.653
Dark red	50 (30.3)	39 (22.0)	0.082	52 (31.5)	38 (21.5)	0.035
Light	0(0)	2 (1.1)	0.509	3 (1.8)	7 (4.0)	0.241
Pink-red	20 (12.1)	19 (10.7)	0.687	21 (12.7)	19 (10.7)	0.567
Pink	1 (0.6)	4 (2.3)	0.411	0(0)	3 (1.7)	0.272
Red	3 (1.8)	10 (5.6)	0.064	0(0)	10 (5.6)	0.005
<b>Vascular tortuosity</b>	4 (2.4)	17 (9.6)	0.006	6 (3.6)	15 (8.5)	0.063
<b>Fog</b>						
Pink dark	104 (63.0)	121 (68.4)	0.299	116 (70.3)	121 (68.4)	0.697
Red dark	17 (10.3)	21 (11.9)	0.646	21 (12.7)	12 (6.8)	0.063
Pink	3 (1.8)	2 (1.1)	0.937	1 (0.6)	0(0)	0.972
Yellow	1 (0.6)	0(0)	0.972	1 (0.6)	2 (1.1)	1.000
Dark yellow	1 (0.6)	1 (0.6)	1.000	0(0)	0(0)	1.000
Pink-red	0(0)	2 (1.1)	0.509	0(0)	1 (0.6)	0.334
<b>Yue yun</b>						
Yellow	1 (0.6)	1 (0.6)	1.000	0(0)	0(0)	1.000
Dark pink	0(0)	0(0)	1.000	0(0)	1 (0.6)	1.000
Red dark	0(0)	0(0)	1.000	1 (0.6)	0(0)	0.972
Tawny	0(0)	0(0)	1.000	1 (0.6)	0(0)	0.972

444 Note, Data presented as mean n (%), P -value < 0.05.

445



446 **Table 3**

447 Comparison of the eye-image features in the CHD group and the control group

Eye-image features	L5		<i>P value</i>	R5		<i>P value</i>
	OR	95% CI		OR	95% CI	
<b>Macula around the black eye</b>	1.608	0.954-2.712	0.075	1.527	0.891-2.616	0.123
<b>Speckle</b>						
Pink dark	4.143	1.135-15.124	0.031	1.620	0.267-9.821	0.600
Red dark	1.812	0.426-7.707	0.421	0.593	0.242-1.453	0.253
Yellow	0.847	0.384-1.868	0.681	1.074	0.214-5.398	0.931
Dark yellow	0.714	0.26-1.962	0.513	1.644	0.572-4.725	0.356
Light	-	-	-	3.302	0.657-16.596	0.147
Grey	-	-	-	-	-	-
Red	-	-	-	2.160	0.194-24.041	0.531
Pink-red	1.073	0.067-17.298	0.960	-	-	-
<b>Spot</b>						
Pink dark	1.298	0.389-4.337	0.672	0.712	0.117-4.313	0.711
Red dark	2.174	0.393-12.029	0.374	1.632	0.452-5.890	0.454
Dark yellow	2.204	0.651-7.461	0.204	0.534	0.048-5.940	0.609
Grey	1.074	0.149-7.710	0.944	1.620	0.267-9.821	0.600
Light	1.074	0.149-7.720	0.944	-	-	-
Red	-	-	-	-	-	-
<b>Mound</b>						
Yellowish	1.577	0.95-2.619	0.078	2.083	1.221-3.554	0.007
Light	1.004	0.575-1.754	0.988	1.291	0.561-2.967	0.548
Dark yellow	0.933	0.44-1.977	0.856	1.632	0.452-5.890	0.454
Grey	0.534	0.048-5.94	0.609	0.759	0.236-2.440	0.643
Pink yellow	0.422	0.081-2.206	0.307	0.531	0.096-2.936	0.468
Pink	1.620	0.267-9.821	0.600	0.902	0.525-1.550	0.708
Dark red	1.073	0.067-17.298	0.960	-	-	-

448

Eye-image features	L5		<i>P value</i>	R5		<i>P value</i>
	OR	95% CI		OR	95% CI	
<b>Blood vessel</b>						
Pink dark	1.214	0.79-1.865	0.376	0.902	0.576-1.413	0.653
Dark red	1.538	0.946-2.502	0.083	1.683	1.035-2.738	0.036
Light	-	-	0.999	0.450	0.114-1.769	0.253
Pink-red	1.147	0.589-2.235	0.687	1.213	0.627-2.347	0.567
Pink	0.264	0.029-2.384	0.235	-	-	-
Red	0.309	0.084-1.144	0.079	-	-	-
<b>Vascular tortuosity</b>	0.234	0.077-0.710	0.010	0.408	0.154-1.077	0.070
<b>Fog</b>						
Pink dark	0.789	0.504-1.234	0.299	1.096	0.691-1.736	0.697
Red dark	0.853	0.433-1.681	0.646	2.005	0.953-4.218	0.067
Pink	1.620	0.267-9.821	0.600	-	-	-
Yellow	-	-	-	0.534	0.048-5.940	0.609
Dark yellow	1.073	0.067-17.298	0.960	-	-	-
Pink red	-	-	-	-	-	-
<b>Yue yun</b>						
Yellow	1.073	0.067-17.298	0.960	-	-	-
Dark pink	-	-	-	-	-	-
Red dark	-	-	-	-	-	-
Tawny	-	-	-	-	-	-

449 Note, The L5 95% and R5 95% represent the 95% lower and upper limits of the OR, respectively. *P* -value < 0.05  
 450

451 **Table 4**

452 analysis of eye-image features using multivariate regression

Variables	OR	95%CI		<i>P value</i>
		lower limit	upper limit	
L5- vascular tortuosity	0.229	0.060	0.873	0.031
Male	2.966	1.727	5.095	<0.001
Age	1.037	1.008	1.068	0.012
Smoking	0.256	0.256	0.829	0.010
Serum glucose	1.260	1.090	1.457	0.002

453