Research Article

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Relationship of Gensini score with retinal vessel diameter and arteriovenous ratio in senile CHD

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Abstract

Background – This study aimed to find the correlation of Gensini score with retinal vessel diameter and arteriovenous ratio in elderly patients with coronary heart disease (CHD).

Methods – This study included 120 senile CHD patients as the CHD group and 100 healthy individuals as the normal group (NG). Gensini score was used to evaluate the severity of coronary artery lesions. Central retinal artery equivalents (CRAE), central retinal venular equivalents (CRVE), and arteriovenous ratio (AVR) were measured.

Results – CHD group has lower CRAE and AVR than NG, while higher CRVE was observed in NG. CRAE and AVR in UAP (unstable angina pectoris) and AMI (acute myocardial infarction) groups showed reduction (stable angina pectoris); however, enhanced CRVE and Gensini scores in UA and AMI groups were observed as compared to the SAP group. CRAE and AVR in moderate and severe groups were reduced to a greater extent compared to the mild groups, while enhanced CRVE and Gensini scores were observed more often in the severe group than the mild group. CRAE and AVR were negatively correlated with the Gensini score; however, CRVE was positively correlated with the Gensini score.

Conclusion – AVR is expected to be a noninvasive index to diagnose and predict senile CHD, which has a certain evaluation value. Diabetes, smoking history, and TC are independent risk factors of senile CHD.

Keywords: CHD in the elderly, Gensini score, retinal vessel diameter, correlation

1 Introduction

Coronary heart disease (CHD) is a familiar cardiovascular disease and chronic disease in the elderly [1]. With the aging of the population and the lifestyle changes, the incidence and mortality of CHD are increasing [2]. Related studies show that CHD incidence increases with age, and a high incidence of CHD is observed in the elderly [3]. The primary pathological basis of CHD is atherosclerosis [4]. Risk factors of CHD include age, genetic factors, hypertension, diabetes, dyslipidemia, overweight, obesity, and smoking. Clinical diagnosis is mainly performed by coronary CT, coronary angiography, and other imaging examinations [5]. Previous studies have reported that senile CHD patients have severe coronary artery stenosis and poor prognosis, which has seriously endangered the physical and mental health of senile CHD patients and reduced their quality of life [6]. Gensini score is an effective index to test the severity of the lesion and can accurately test the patient’s condition [7]. In the past, many studies explored the methods of predicting and evaluating the lesions, mainly including the determination of many biomarkers such as vascular-related inflammatory factors, growth differentiation factors, and angiopoietin-like proteins in the body, and imaging techniques such as coronary angiography [8–10]. However, there are some disadvantages such as high cost and trauma to the body of these methods [11]. Therefore, it is of great clinical significance to find a simple, noninvasive, convenient, economic, and repeatable detection index for an early and accurate evaluation of the degree of lesions to prevent senile CHD.

Many blood vessels in a typical organism have certain similarities in hemodynamic effects and metabolic environment, so the possibilities of developing certain types of diseases in these blood vessels are also similar [12,13]. More and more studies show that atherosclerosis is a systemic arterial disease, and microangiopathy acts in the pathogenesis of CHD [14,15]. Retinal vessels are the only vessels that can be directly observed by noninvasive methods, which provides a good option to test the microvascular function of the whole body [16,17]. As retinal
vessels and coronary arteries have similar anatomical and physiological characteristics, the change of their diameters may indicate structural damage or functional changes, which has a particular early warning effect on CHD [18]. Color fundus photography allows to observe the pathological changes of retinal vessels and their surrounding tissues through the pupil, quantitatively analyze the diameter of retinal blood vessels with the aid of auxiliary software, record and save imaging data, facilitate systematic observation and analysis, and have the advantages of noninvasive safety, reliable information, simplicity, and low cost, which can provide important information for observing and studying the structure and functional states of body blood vessels [19,20].

In this study, the authors have taken color fundus photography for senile CHD patients, directly measured the diameter of retinal artery and vein with the help of computer technology, calculated the ratio of artery and vein, and discussed their correlation with Gensini score.

2 Materials and methods

2.1 General data

Altogether 120 senile CHD patients from January 2017 to June 2019 were selected as the CHD group, including 72 men and 48 women, aged 60–72 years, with an average of 65.25 ± 4.92 years. Inclusion criteria of this study were as follows: the diagnosis conformed to the diagnostic criteria of CHD formulated by WHO; the lesions were determined by coronary angiography, which showed that the primary branch stenosis was ≥50% or the secondary branch stenosis was ≥75%; and the lesion severity was determined by the Gensini method. According to different clinical types, patients with CHD were grouped into SAP, UA, and AMI. According to the Gensini score, patients with CHD were grouped into mild with 1–30 points, moderate with 31–60 points, and severe with 60 points. Exclusion criteria of this study were as follows: patients with eye refractive system diseases cannot be examined with ocular fundus; patients with congenital ocular vascular diseases; patients with a malignant tumor, autoimmune disease, infectious disease, and severe organ dysfunction; patients with acute and chronic infection; patients with mental illness; and patients without complete clinical data. Besides this, 100 healthy people in our hospital were selected as the normal group (NG), including 58 men and 42 women, aged 60–70 years, with an average of (65.58 ± 5.02) years.

Informed consent: Informed consent has been obtained from all individuals included in this study.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies, and in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors’ institutional review board or equivalent committee.

2.2 Examination method

2.2.1 Coronary angiography and assessment of the degree of vascular lesion

All patients with CHD were examined by coronary angiography using Philips CV Integris angiography machine with standard right femoral artery approach or right radial artery approach. Each lesion was determined by more than two orthogonal project positions, and the stenosis degree was expressed by the percentage of coronary artery diameter stenosis. Two cardiovascular interventional physicians determined the results. According to the location and degree of the lesion, the score was calculated by Gensini score standard to test the extent and severity of ischemia caused by the lesion.

Gensini score evaluation criteria [21] were as follows: Gensini score is the sum of coronary stenosis degree score and lesion site score. Stenosis degree score was as follows: the stenosis degree between 1 and 25% was recorded as 1 point; 26–50% as 2 points; 51–75% as 4 points; 76–90% as 8 points; 91–99% as 16 points; and 100% as 32 points. The lesion score is the product of a single lesion score and coefficient: the coefficient indicates the importance of stenosis in different positions of the coronary artery system, and the coefficients of each site are as follows: left trunk: 5, proximal left anterior descending branch: 2.5, middle left anterior descending branch: 1.5, aorta and first diagonal branch: 1, second diagonal branch: 0.5, distal left anterior descending branch: 1; the proximal left circumflex branch: 2.5, the middle left circumflex branch: 2.5, the distal left circumflex branch: 1, the blunt edge branch: 0.5; the proximal segment of a right coronary artery: 1, the middle segment of a right coronary artery: 1, the distal segment of a right coronary artery: 1, posterior descending branch: 1, the posterior branch of the left ventricle: 0.5. Gensini score with 1–30 points was regarded as mild; 31–60 as moderate; and >60 as severe.
2.2.2 Measurement of retinal vessel diameter

All participants were examined by fundus photography: compound tropicamide eye drops were given to mydriasis, one drop each time, with an interval of 15 min, and the eyes were dropped twice in total, and fundus photography was performed 30 min later. The steps were performed by an experienced ophthalmologist using a Topcon fundus camera in Japan in a dark room, and a 45° elevation angle of both eyes centered on the fovea of optic disc and macula was selected, and the retinal images of both eyes were obtained and stored. The retinal vessel diameter was measured by IVAN software (University of Wisconsin, Madison): in the area of 0.5–1 DD away from the edge of the optic disc in color fundus photographs, the blood vessel diameters of six large retinal artery and vein branches were automatically identified and measured by the software. Par–Hubbard–Knudtson correction formula was applied to calculate the central retinal artery equivalent (CRAE), central retinal vein equivalent (CRVE), and the arteriovenous ratio (AVR) = CRAE/CRVE.

2.2.3 Blood biochemical indicators

A fasting venous blood sample was obtained after 12 h on an empty stomach, and blood lipids were detected by Roche modular automatic biochemical analyzer, along with total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

2.3 Statistical method

SPSS 20.0 was applied for the statistical analysis, and Graph Pad Prism 6 for visualizing the figures. The measurement data was represented by mean ± SD and compared by independent sample t-test. The comparison before and after treatment was made by paired t-test. The multiple comparisons were made by one-way ANOVA, and the pairwise comparison among groups was made by the SNK-q test. Counting data were represented by several cases/percentage [n (%)] and compared by the Chi-square test. When the theoretical frequency in the Chi-square test was less than 5, the continuity correction Chi-square test was applied. ROC was applied to test the diagnostic value of AVR in patients with CHD. Pearson correlation coefficient was applied to analyze the correlation of Gensini score with CRAE, CRVE, and AVR. Multivariate logistic regression was applied to analyze the risk factors affecting the severity of the lesions in patients with CHD. P < 0.05 indicated statistical difference.

3 Results

3.1 General data

There was no evident difference in sex, age, history of hypertension, diabetes, drinking, smoking, TC, TG, HDL-C, and LDL-C between the CHD and NG (P > 0.05; Table 1).

3.2 Comparison of CRAE, CRVE, and AVR between CHD group and NG

CRAE, CRVE, and AVR in the CHD group were reduced compared to those in the NG group (P < 0.05; Figure 1).

| Category | n   | CHD group | NG | χ2/t | P   |
|----------|-----|-----------|----|------|-----|
| Gender   |     | (n = 120) |     |      |     |
| Male     | 130 | 58 (58.00) | 72 (60.00) | 0.090 | 0.763 |
| Female   | 90  | 42 (42.00) | 48 (40.00) |      |      |
| Age (years) | 220 | 65.58 ± 5.02 | 65.25 ± 4.92 | 0.490 | 0.624 |
| History of hypertension | No  | 116  | 54 (54.00) | 62 (51.67) | 0.119 | 0.730 |
| Yes      | 104 | 46 (46.00) | 58 (48.33) |      |      |
| History of diabetes | No  | 160  | 72 (72.00) | 88 (73.33) | 0.048 | 0.825 |
| Yes      | 60  | 28 (28.00) | 32 (26.67) |      |      |
| Drinking history | No  | 170  | 78 (78.00) | 92 (76.67) | 0.055 | 0.814 |
| Yes      | 50  | 22 (22.00) | 28 (23.33) |      |      |
| Smoking history | No  | 119  | 55 (55.00) | 64 (53.33) | 0.061 | 0.804 |
| Yes      | 101 | 45 (45.00) | 56 (46.67) |      |      |
| Gensini score (Points) | 1–30 | 40  | — | 40 (33.33) |      |      |
|         | 31–60 | 45  | — | 45 (37.50) |      |      |
|         | >60  | 35  | — | 35 (29.17) |      |      |
| TC (mmol/L) | 220 | 4.50 ± 0.40 | 4.56 ± 0.42 | 1.078 | 0.282 |
| TG (mmol/L) | 220 | 1.34 ± 0.21 | 1.38 ± 0.27 | 1.208 | 0.228 |
| HDL-C (mmol/L) | 220 | 1.15 ± 0.16 | 1.18 ± 0.17 | 1.338 | 0.182 |
| LDL-C (mmol/L) | 220 | 3.02 ± 0.32 | 3.09 ± 0.36 | 1.510 | 0.132 |
Figure 1: Comparison of CRAE, CRVE, and AVR between CHD group and NG. (a) CRAE in CHD group was reduced than that in NG. (b) CRVE in CHD group was larger than that in NG. (c) AVR in CHD group was reduced than that in NG. Note: ***$P < 0.001$. 

Figure 2: Comparison of CRAE, CRVE, AVR, and Gensini scores in different CHD groups. (a) CRAE in UA and AMI groups was reduced than that in the SAP group, while CRAE in the AMI group was reduced than that in the UA group. (b) CRVE of the UA group and the AMI group was enhanced than that of the SAP group, while CRVE of the AMI group was enhanced than that of the UA group. (c) AVR of the UA group and AMI group was reduced than that of the SAP group, while AVR of the AMI group was reduced than that of the UA group. (d) The Gensini score of the UA group and AMI group was enhanced than that of the SAP group, while the Gensini score of AMI group was enhanced than that of the UA group. Note: ***$P < 0.001$. 
3.3 Comparison of CRAE, CRVE, AVR, and Gensini scores in different CHD groups

CRAE and AVR in UA and AMI groups were reduced compared to those in the SAP group \((P < 0.05)\), while CRVE and Gensini scores in UA and AMI groups were enhanced compared to those in the SAP group \((P < 0.05; \text{Figure 2})\).

3.4 Comparison of CRAE, CRVE, AVR, and Gensini scores in different Gensini score groups

CRAE and AVR in moderate and severe groups were reduced compared to those in the mild group \((P < 0.05)\), while CRVE and Gensini scores in the severe group were enhanced compared to those in the mild group \((P < 0.05; \text{Figure 3})\).

3.5 Diagnostic value of AVR in patients with CHD

By visualizing the ROC curve analysis, it was found that the AUC of AVR in diagnosing CHD was 0.815 \((95\% \text{ CI: } 0.757–0.874)\), the cutoff value was 0.77, the diagnostic sensitivity was 92.00\%, and the specificity was 60.00\% (Table 2 and Figure 4).

![Figure 3](image-url) (a) CRAE of moderate and severe groups was reduced than that of the mild group, and CRAE of the severe group was reduced than that of the moderate group. (b) CRVE of moderate and severe groups was enhanced than that of the mild group, and CRVE of the severe group was enhanced than that of the moderate group. (c) AVR of the moderate and severe groups was reduced than that of the mild group, while AVR of the severe group was reduced than that of the moderate group. (d) Gensini scores in moderate and severe groups were enhanced than those in the mild group, and those in the severe group were enhanced than those in the moderate group. Note: ***\(P < 0.001\).
3.6 Correlation of CRAE, CRVE, and AVR with Gensini score

Pearson correlation coefficient was applied to analyze the correlation of CRAE, CRVE, and AVR with Gensini score in CHD patients. The results showed that CRAE and AVR had a negative correlation with Gensini score \( r = -0.612, P < 0.001; r = -0.773, P < 0.001 \) and CRVE had a positive correlation with Gensini score \( r = 0.414, P < 0.001 \); Figure 5).

![Figure 4: ROC curve of AVR diagnosing CHD. The sensitivity and specificity of AVR in diagnosing CHD were 92.00 and 60.00%, respectively.](image)

3.7 Risk factors of coronary stenosis in patients with CHD

The current study involves 40 CHD patients with Gensini score ≤30 as a good group and 80 CHD patients with Gensini score >30 as a bad group. After univariate analysis, the authors found that there was no evident difference in gender, average age, history of hypertension, drinking, TG, HDL-C, and LDL-C \( P > 0.05 \), but there were evident differences in diabetes, smoking, and TC \( P < 0.05 \); Table 3).

Diabetes history, smoking history, and TC were included in the analysis, and they were assigned as independent variables. Taking the degree of coronary stenosis as the dependent variable, the logistic regression model was applied to carry out a multivariate analysis. The results showed that diabetes history, smoking history, and TC were independent risk factors for CHD patients (Tables 4 and 5).

4 Discussion

CHD refers to coronary artery disease syndrome caused by the insufficient blood supply to the heart and coronary artery stenosis \[22\]. The morbidity and fatal disability rates are very high, causing great harm to patients’ lives.
Table 3: Univariate analysis of coronary stenosis degree in CHD patients [n (%), mean ± SD]

| Factor                   | Good group (n = 40) | Bad group (n = 80) | χ²/t   | P     |
|--------------------------|---------------------|--------------------|--------|-------|
| Gender                   |                     |                    |        |       |
| Male                     | 72 (55.00)          | 50 (62.50)         | 0.625  | 0.429 |
| Female                   | 48 (45.00)          | 30 (37.50)         |        |       |
| Average age (years)      | 120 ± 4.52          | 65.45 ± 4.92       | 1.720  | 0.089 |
| History of hypertension |                     |                    |        |       |
| No                       | 62 (25.50)          | 37 (46.25)         | 0.417  | 0.518 |
| Yes                      | 58 (47.50)          | 43 (53.75)         |        |       |
| History of diabetes      |                     |                    | 6.158  | 0.013 |
| No                       | 88 (35.75)          | 53 (66.25)         |        |       |
| Yes                      | 32 (12.50)          | 27 (33.75)         |        |       |
| Drinking history         |                     |                    | 0.582  | 0.445 |
| No                       | 92 (72.50)          | 63 (78.75)         |        |       |
| Yes                      | 28 (27.50)          | 17 (21.25)         |        |       |
| Smoking history          |                     |                    | 4.838  | 0.027 |
| No                       | 64 (27.50)          | 37 (46.25)         |        |       |
| Yes                      | 56 (32.50)          | 43 (53.75)         |        |       |
| TC (mmol/L)              | 120 4.12 ± 0.38     | 4.91 ± 0.50        | 8.121  | 0.001 |
| TG (mmol/L)              | 120 1.33 ± 0.20     | 1.42 ± 0.28        | 1.686  | 0.095 |
| HDL-C (mmol/L)           | 120 1.08 ± 0.14     | 1.14 ± 0.16        | 1.829  | 0.070 |
| LDL-C (mmol/L)           | 120 2.97 ± 0.32     | 3.10 ± 0.37        | 1.722  | 0.088 |

and health, and it has become a common public health problem of fatal diseases [23]. Therefore, it is of great significance to detect and monitor the progress of the disease in time and judge the severity of the lesions for the prevention and treatment of CHD [24,25]. This study predicted and tested the severity of the lesions in CHD patients by quantitatively measuring the diameter of retinal blood vessels.

Previous research has shown that the change of retinal vessel diameter is related to hypertension, diabetes, and cerebrovascular diseases and has a particular suggestive effect on CHD [26,27]. However, few reports are available on the correlation of retinal vessel diameter with CHD. The results showed that CRAE and AVR of CHD patients were lower than those of normal people, while CRVE was higher than that of normal people, indicating that the retinal artery of senile CHD patients was narrowed, the vein was dilated, and the ratio of artery and vein became smaller. Chandra et al. [28] revealed that retinal artery stenosis and vein dilatation were related to atherosclerotic heart failure, and the risk of occurrence could be predicted. In the study by Anyfanti et al. [29], it was reported that the retinal artery of rheumatoid arthritis patients was smaller than that of the healthy people, which was related to inflammatory reaction and could play a predictive role in cardiovascular disease. The authors further analyzed CRAE, CRVE, AVR, and Gensini scores of patients with CHD in different clinical types and pathological degrees. The results showed that CRAE and AVR scores of patients with UA and AMI were smaller than those of SAP, while CRVE and Gensini scores were higher than those of SAP. CRAE and AVR of severe and mild patients were lower than those of mild patients, and CRVE and Gensini scores were higher than those of mild patients [30]. With the severity of CHD, CRVE and Gensini scores were reduced, while CRVE and Gensini scores were enhanced. The correlation of CRAE, CRVE, and AVR with Gensini score was analyzed by the Pearson correlation coefficient. The results show that CRAE and AVR had a negative correlation with the Gensini score, while CRVE was positively correlated with the Gensini score, indicating that the low CRAE and AVR were related to the high CRVE. That suggested that with the deterioration of CHD, the comprehensive index of AVR was more correlated with the Gensini score. In the research of Kim et al. [31], it was suggested that compared with the control group, patients with retinal artery occlusion had an enhanced prevalence of subclinical coronary artery diseases and more extensive coronary artery lesions. Also, in the study by Wang et al. [32], retinal blood vessels were related to CAD degree and Gensini score, which was similar to our research results. The study of the retinal vascular system in senile dementia found a certain correlation between retinal vascular disease and cerebrovascular disease, and retinal vascular characteristics can be applied as a noninvasive index for diagnosis and prognosis of dementia patients [33]. As a comprehensive evaluation index of retinal vascular disease, AVR not only reflects the reduction of retinal

Table 4: Logistic multivariate regression analysis assignment

| Factor                   | Variable | Assignment                        |
|--------------------------|----------|-----------------------------------|
| History of diabetes      | X1       | None = 0, yes = 1                 |
| History of smoking       | X2       | None = 0, yes = 1                 |
| TC                       | X3       | The data belong to continuous variables and are analyzed with original data |
Table 5: Multivariate analysis of coronary stenosis degree in CHD patients

| Factor               | β     | SE   | Wald | P     | OR   | 95% CI          |
|----------------------|-------|------|------|-------|------|-----------------|
| History of diabetes  | 1.968 | 0.624| 14.529 | <0.001| 7.218 | 3.538–17.358   |
| History of smoking   | 2.391 | 0.434| 28.682 | <0.001| 10.127| 5.357–23.505   |
| TC                   | 1.031 | 0.271| 29.895 | <0.001| 3.845 | 2.062–7.140    |

5 Conclusion

To sum up, CRA and AVR are negatively correlated with the Gensini score, while CRVE is positively correlated with the Gensini score. Therefore, AVR is expected to be a noninvasive index to diagnose and predict senile CHD, which has a particular evaluation value. In addition, diabetes, smoking history, and TC are independent risk factors of senile CHD.

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References

[1] Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016;4:256.
[2] Mack M, Gopal A. Epidemiology, traditional and novel risk factors in coronary artery disease. Cardiol Clin. 2014;32:323–32.
[3] Ferreira-Gonzalez I. The epidemiology of coronary heart disease. Rev Esp Cardiol (Engl Ed). 2014;67:139–44.
[4] Chand Negi P, Mahajan K, Merwaha R, Asotra S, Sharma R. Epidemiological trends of the acute coronary syndrome in Shimla district of the hilly state of Northern India: Six-year data from the prospective Himachal Pradesh acute coronary syndrome registry. Indian Heart J. 2019;71:440–5.
[5] Abdar M, Ksiazek W, Acharya UR, Tan RS, Makarenkov V, Plawiak P. A new machine learning technique for an accurate diagnosis of coronary artery disease. Comput Methods Programs Biomed. 2019;179:104992.
[6] Catalan-Serra P, Campos-Rodriguez F, Reyes-Nunez N, Selma-Ferrer MJ, Navarro-Soriano C, Ballester-Canelles M, et al. Increased incidence of stroke, but not coronary heart disease, in elderly patients with sleep apnea. Stroke. 2019;50:491–4.
[7] Li XT, Fang H, Li D, Xu FQ, Yang B, Zhang R, et al. Association of platelet to lymphocyte ratio with in-hospital major adverse cardiovascular events and the severity of coronary artery disease assessed by the Gensini score in patients with acute myocardial infarction. Chin Med J (Engl). 2020;133:415–23.
[8] Ipek E, Ermis E, Uysal H, Kızılel Kül, Demirel S, Yıldırım E, et al. The relationship of micronucleus frequency and nuclear division index with coronary artery disease SYNTAX and Gensini scores. Anatol J Cardiol. 2017;17:483–9.
[9] Alan B, Akpolat V, Akcan A, Alan S. Relationship between osteoprogenic syndrome and severity of coronary artery disease detected with coronary angiography and Gensini score in men. Clin Interv Aging. 2016;11:377–82.
[10] Avci A, Fidan S, Tabakci MM, Toprak C, Alizade E, Acar E, et al. Association between the gensini score and carotid artery stenosis. Korean Circ J. 2016;46:639–45.
Li M, Li L, Wu W, Ran H, Zhang P. Left ventricular dyssynchrony in coronary artery disease patients without regional wall-motion abnormality: correlation with Gensini score. Echocardiography. 2019;36:1689–97.

Bek T. Diameter changes of retinal vessels in diabetic retinopathy. Curr Diab Rep. 2017;17:82.

Kochli S, Endes K, Infanger D, Zahner L, Hanssen H. Obesity, blood pressure, and retinal vessels: a meta-analysis. Pediatrics. 2018;6:141.

Gistera A, Hansson GK. The immunology of atherosclerosis. Nat Rev Nephrol. 2017;13:368–80.

Kattoor AJ, Pothineni NVK, Palagiri D, Mehta JL. Oxidative stress in atherosclerosis. CurrAtheroscler Rep. 2017;19:42.

Li LJ, Ikram MK, Wong TY. Retinal vascular imaging in early life: insights into processes and risk of cardiovascular disease. J Physiol. 2016;594:2175–203.

Xu BL, Zhou WL, Zhu TP, Cheng KY, Li YJ, Zhan HJ, et al. A full maximum method to assess retinal vascular structural changes in patients with ischemic heart disease and microvascular angiography. Sci Rep. 2019;9:11019.

Newman AR, Andrew NH, Casson RJ. Review of pediatric retinal microvascular changes as a predictor of cardiovascular disease. Clin Exp Ophthalmol. 2017;45:33–44.

Pead E, Megaw R, Cameron J, Fleming A, Dhillon B, Trucco E, et al. Automated detection of age-related macular degeneration in color fundus photography: a systematic review. SurvOphthalmol. 2019;64:498–511.

Kashani H, Zeraati H, Mohammad K, Goodarzynjead H, Mahmoudi M, Sadeghian S, et al. Analyzing Gensini score as a semi-continuous outcome. J Tehran Heart Cent. 2016;11:55–61.

Shrivastava U, Misra A, Mohan V, Unnikrishnan R, Bachani D. Obesity, diabetes and cardiovascular diseases in India: public health challenges. Curr Diabetes Rev. 2017;13:65–80.

Satija A, Bhupathiraju SN, Spiegelman D, Chiue SE, Manson JE, Willett W, et al. Healthful and unhealthful plant-based diets and the risk of coronary heart disease in U.S. adults. J Am Coll Cardiol. 2017;70:411–22.

Long T, Peng L, Li F, Xia K, Jing R, Liu X, et al. Correlations of DAPT score and PRECISE-DAPT score with the extent of coronary stenosis in acute coronary syndrome. Medicine (Baltimore). 2018;97:e12531.

Tselios K, Sheane BJ, Gladman DD, Urowitz MB. Optimal monitoring for coronary heart disease risk in patients with systemic lupus erythematosus: a systematic review. J Rheumatol. 2016;43:54–65.

Wang J, Jiang J, Zhang Y, Qian YW, Zhang JF, Wang ZL. Retinal and choroidal vascular changes in coronary heart disease: an optical coherence tomography angiography study. Biomed Opt Express. 2019;10:1532–44.

Poplin R, Varadarajan AV, Blumer K, Liu Y, McConnell MV, Corrado GS, et al. Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. Nat Biomed Eng. 2018;2:158–64.

Chandra A, Seidelmann SB, Claggett BL, Klein BE, Klein R, Shah AM, et al. The association of retinal vessel calibers with heart failure and long-term alterations in cardiac structure and function: the atherosclerosis risk in communities (ARIC) study. Eur J Heart Fail. 2019;21:1207–15.

Anyfantis P, Triantafyllou A, Gkaliagkousi E, Koletssos N, Athanasopoulos G, Zabulis X, et al. Retinal vessel morphology in rheumatoid arthritis: association with systemic inflammation, subclinical atherosclerosis, and cardiovascular risk. Microcirculation. 2017;24(8).

Richards SH, Anderson L, Jenkinson CE, Whalley B, Rees K, Davies P, et al. Psychological interventions for coronary heart disease. Cochrane Database Syst Rev. 2017;4:CD002902.

Kim YD, Kim YK, Yoon YE, Yoon CH, Park KH, Woo SJ. Association of retinal artery occlusion with subclinical coronary artery disease. J Korean Med Sci. 2019;34:e286.

Wang SB, Mitchell P, Liew G, Wong TY, Phan K, Thiagalingam A, et al. A spectrum of retinal vasculature measures and coronary artery disease. Atherosclerosis. 2018;268:215–24.

McGrory S, Cameron JR, Pellegrini E, Warren C, Doubl FN, Deary II, et al. The application of retinal fundus camera imaging in dementia: a systematic review. Alzheimers Dement (Amst). 2017;6:91–107.

Gururani K, Jose J, George PV. Testosterone as a marker of coronary artery disease severity in middle-aged males. Indian Heart J. 2016;68(Suppl 3):S16–20.