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Retinal vascular fingerprints predict incident stroke: findings from UK Biobank cohort study

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Abstract

Objective: To investigate the associations between a comprehensive set of retinal vascular parameters and incident stroke to unveil new associations and explore its predictive power for stroke risk.

Methods: Retinal vascular parameters were extracted from the UK Biobank fundus images using the Retina-Based Microvascular Health Assessment System. We used Cox regression analysis, adjusted for traditional risk factors, to examine the associations, with False Discovery Rate adjustment for multiple comparisons. Receiver Operating Characteristic Curves were used to assess their predictive values.

Results: During a median follow-up of 12.5 years, 749 incident strokes occurred among 45,161 participants. The analysis identified 29 significant parameters associated with stroke risk, with a notable dominance of Density parameters (over half). Each standard deviation (SD) change in these parameters increased stroke risk by 9.8% to 19.0%. For identified Calibre parameters, each SD change was associated with an increased risk (ranging from 10.1% to 14.1%). For identified Complexity parameters and arterial Inflection Count Tortuosity, each SD decrease was linked to an increased risk (ranging from 10.4% to 19.5%). The introduction of retinal vascular parameters improved the Area Under the Receiver Operating Characteristic Curve to 0.752, significantly outperforming the model using only traditional risk factors (0.739, P<0.001).

Conclusions: Retinal vascular analysis, a non-invasive screening approach for stroke risk assessment, performed better than traditional risk stratification models. The 29 novel retinal indicators identified offer new avenues for stroke pathophysiology research.

Keywords:

Retinal vascular parameters, Incident stroke, Risk prediction, Cohort study, Retina-Based Microvascular Health Assessment System

What is already known:
While previous studies have identified a link between retinal blood vessel features and stroke risk, they primarily focused on a limited range of vascular parameters such as diameter, fractal dimension, and tortuosity, and findings using these approaches have often been inconsistent. Traditional stroke risk assessment methods such as blood tests can be invasive or expensive and also are limited in their prediction success. Improved stroke prediction models are needed and novel approaches to retinal vessel analysis offer the possibility of improved prediction accuracy.

What this study adds:
This study applied an advanced algorithm, Retina-Based Microvascular Health Assessment System (RMHAS), to analyze a comprehensive set of retinal vascular parameters (118 parameters in total) using fundus photos from a large well-studied cohort (UK Biobank). We conducted separate evaluations of arteries and veins, as well as network features within and outside the macular region. We identified 29 novel retinal indicators significantly associated with stroke risk, with a dominance of Density-related parameters. Importantly, when combined with age and sex, the newly identified retinal parameters had comparable predictive power for stroke risk when compared to established traditional risk factors. Given that age and sex are readily available, and retinal parameters can be obtained through routine fundus photography; this model presents a practical and easily implementable approach for incident stroke risk assessment, particularly for primary health care and low-resource settings.

How this study might affect research, practice, or policy:
Further investigation of identified parameters, especially Density parameters, may provide valuable insights into the intricate pathophysiological processes associated with stroke. The non-invasive nature of retinal analysis paves the way for easier, more accessible stroke risk screening, especially in primary care settings. This approach could inform future policy regarding stroke prevention strategies, potentially leading to earlier intervention and improved patient outcomes.

Introduction

Stroke is one of the most common cardiovascular diseases and results in approximately 6.7 million deaths annually[1]. While stroke affects over 100 million people worldwide[2], nearly 90% are attributable to modifiable risk factors like hypertension, high cholesterol, diet, and smoking[3]. Therefore, early identification of individuals at risk could empower earlier intervention, thereby reducing stroke-related disability and mortality.

The intricate retinal vascular network is known to share common anatomical and physiological features with the vasculature of the brain[4] allowing for a non-invasive assessment of vasculature health. Previous studies have shown that retinal microvascular abnormalities in the form of tortuosity, venous calibre, arteriovenous nicking, and microaneurysms reflect damage from systemic conditions, such as hypertension, diabetes, and hypercholesterolemia[5,6], all of which are known modifiable risk factors for stroke[7]. There are also studies showing that retinal anatomical features such as fractal dimension, tortuosity, and calibre are markers of future mortality from stroke[8].

However, the link between retinal vascular parameters and incident stroke has not resulted in the widespread use of fundus photography to improve risk prediction. This gap arises from inconsistent study findings as well as imperfect risk prediction[9-11]. The variability in findings underscores the need to identify more accurately the optimal biomarkers for future stroke. The advent of new extraction methods for these parameters, facilitated by deep learning models like the Retina-Based Microvascular Health Assessment System (RMHAS)[12], allows for better use of fundus photographs to determine risk. These analyses could provide a more nuanced understanding of specific vascular factors associated with stroke, uncovering previously overlooked indicators. Furthermore, traditional predictors such as glucose level, cholesterol level, or other lab tests[13] require invasive blood tests, posing practical challenges associated with increased cost and reduced feasibility for large-scale screening. Fundus imaging is non-invasive, offering a more simplified approach to screening[14-16].

We used RMHAS[12] to extract retinal vascular parameters from fundus images from the UK Biobank study. We aimed to identify previously unknown associations between geometric vascular features and incident stroke risk, to examine the added predictive value of parameters generated with RMHAS, and to provide insight into specific vascular patterns associated with increased stroke risk.

Methods

Study population

We used data from the UK Biobank, a large prospective cohort study, and followed STROBE (STrengthening the Reporting of OBservational studies in Epidemiology)[17] guidelines. The UK Biobank study enrolled participants aged 40 to 69 across the United Kingdom from 2006 to 2010 at baseline. The data, including demographic information, lifestyle factors, and medical conditions, were collected via questionnaires and examinations at baseline and follow-up visits and linked from national health registries with regular updates[18]. In 2009, eye examinations were introduced, with about 60,000 participants receiving eye examinations at baseline and about 20,000 receiving eye assessments between 2012 and 2013[19]. A total of 68,753 participants with fundus images were included in the current study.

Ethical consideration

The ethical approval for the UK Biobank study was obtained from the North-West Multi-Centre Research Ethics Committee (06/MRE08/65), and informed consent was obtained.

Ascertainment of variables

The retinal vascular parameters were obtained using RMHAS[12], a deep learning algorithm for automated segmentation and quantification of retinal vascular networks. The image quality was categorized as “good”, “usable”, and “reject”. The rejected images were considered ungradable and excluded from further analysis.[12] A total of 30 measure types of 5 categories: Calibres, Density, Tortuosity, Branching Angle, and Complexity, were extracted. (Figure 1) To minimize the potential impact of extreme values, we excluded outliers following the method proposed by Zekayat et al[20].

Demographic and socioeconomic factors, including age, sex, and social deprivation, were obtained via questionnaire. The Indices of Multiple Deprivation (IMP) was used to indicate social deprivation. Lifestyle factors and health parameters, including blood pressure, low-density lipoprotein (LDL), high-density lipoprotein (HDL), cholesterol, glycosylated hemoglobin (HbA1c), body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP), were used as potential confounders[7]. SBP and DBP were taken twice using an Omron device, and the mean value was used in our study. LDL, HDL, and cholesterol levels were measured by enzyme immunoinhibition analysis on a Beckman Coulter AU5800. HbA1c was measured by HPLC analysis on a Bio-Rad VARIANT II Turbo. (Supplementary Table 1)

Outcome definition

We identified medical conditions using the International Classification of Diseases, edition 10 (ICD-10) and ICD-9. Incident stroke, the primary outcome, was identified using ICD-10 codes “I60, I61, I63, I64, I67, I69” and ICD-9 codes “4309, 4319, 4349, 4369”. The data were obtained through linkage and updated regularly. https://biobank.ndph.ox.ac.uk/showcase/exinfo.cgi?src=Data_providers_and_dates shows details. Participants with stroke, peripheral vascular disease, heart attack, myocardial infarction, heart failure, or cancer at baseline were excluded.

(Supplementary Table 1) Additionally, we excluded those who died or had a stroke attack within the first year of follow-up to minimize the influence of reverse causality and selection bias. The image acquisition date was the baseline date, and the end date was the date of death or stroke attack, or 31 October 2022, whichever came first.

Statistical analysis

For the association analysis, we adopted Cox proportional hazard regression to account for the time-to-event duration. We rescaled values of retinal vascular parameters to standard deviation (SD) units. Multivariate Imputation by Chained Equations was used for imputation.

In the adjusted model, we adjusted for traditional risk factors[7], including age, sex, IMP, SBP, total cholesterol, HDL, HbA1c, smoking, and BMI. In both models, the False Discovery Rate (FDR) method was used to adjust P values. Furthermore, to test non-linear associations, we divided parameters into quintiles to examine as categorical variables and used the Restricted Cubic Spline.

To assess the robustness of our findings, we performed three sensitivity analyses: 1) Focusing on participants with over three years of follow-up; 2) Including those with valid retinal images and cardiovascular risk; 3) Adjusting for spherical equivalent refractive error. Subgroup analyses were performed by age, gender, smoking status, and presence of diabetes, obesity, and hypertension.

Furthermore, we explored the added predictive value of retinal vascular parameters. To address potential multicollinearity, we calculated the Variance Inflation Factor (VIF) and excluded features with high VIF values (>10). Subsequently, we employed the receiver operating characteristic (ROC) curves to assess their predictive performance and calculated the area under the curve (AUC).

A two-tailed P value of 0.05 was set for statistical significance for all analyses, and R 4.2.3 was used to perform analyses.

Results

Characteristics of participants

Among 51,390 participants with eligible images, 6,189 participants were excluded due to a history of stroke, heart disease, peripheral vascular disease, or cancer. An additional 40 participants were excluded because their follow-up duration was one year or less. This resulted in a final analysis population of 45,161 participants. Figure 2 presents the exclusion and inclusion of participants at each stage, with Supplementary Table 2 showing characteristics of those included and excluded.

A total of 749 incident events were observed during a median follow-up time of 12.5 (interquartile range: 12.3-12.6) years. Participants who experienced an incident stroke were significantly older (61.3±6.8 years vs 55.3±8.2 years, p<0.001), more likely to be male (54.3% vs 45.0%, p<0.001), current smokers (12.8% vs. 8.9%; P<0.001), and have diabetes (9.6% vs. 3.8%; P<0.001), Table 1. Among health measures, a statistically higher BMI, DBP, and SBP, and a lower HDL were found in the incident stroke group (all P-values < 0.001).

Association with incident stroke

A total of 118 retinal vascular parameters were included in the Cox regression models. Among those, 29 parameters were significantly associated with incident stroke risk after controlling for traditional risk factors and FDR adjustment (Figure 3). It's noteworthy that over half (17) of those parameters were Density parameters. Additionally, there were 8 Complexity parameters, 3 Calibre parameters, and 1 Tortuosity parameter.

Calibre

Among the 5 Calibre measure types, only Central Retinal Artery Equivalent (CRAE) and parameters of Length Diameter Ratio (LDR) were significantly associated with the risk of incident stroke in the fully adjusted model. One SD increase in CRAE was associated with a 9.4% decrease in stroke risk, with a hazard ratio (HR) of 0.906 (95% CI: 0.840-0.976, p=0.04). Namely, each SD decrease in CRAE was associated with a 10.4% stroke risk increase (HR = 1/0.906 = 1.104). Additionally, each SD increase in arterial LDR and LDR of vessels in the macula increased the risk of stroke by 14.1% and 10.1%, with HRs of 1.141 (95% CI: 1.066-1.221, p<0.01) and 1.101 (95% CI: 1.030-1.177, p=0.03) respectively.

Complexity

Each SD decrease in Fractal Dimension (FD) and arterial FD was associated with 12.4% (1/0.890 = 1.124) and 16.0% (1/0.862 = 1.160) risk increase, respectively. Additionally, a one SD decrease in the Number of Bifurcation Points, Branching Points, and Segments of arteries and vessels in the macular region increased the risk of stroke by 10.4% to 16.8% (1/0.906 = 1.104 to 1/0.856 = 1.168).. Furthermore, a one SD decrease in the Number of nonterminal points and terminal points in arteries increased the risk of stroke by 15.9% (1/0.863 = 1.159) and 17.5% (1/0.851 = 1.175), respectively.

Density

Seventeen Density parameters were associated with incident stroke risk. Each SD increase in the Arc Length in arteries, vessels within the macular region, terminal arteries, and non-terminal arteries was associated with an increased stroke risk (ranging from 9.8% to14.4%), with HRs ranging from 1.098 to 1.144. Similarly, a one SD increase in Chord Length in arteries and vessels within the macular region increased the risk by 13.4% and 12.2%, exhibiting HRs of 1.134 (95%CI: 1.060-1.214, p<0.01) and 1.122 (95%CI: 1.050-1.198, p<0.01).

Notably, decreases in other identified Density parameters were all associated with increased stroke risk. Specifically, one SD decrease in arterial Bifurcation Density increased risk by 10.7%, and one SD decrease in Branching Density in arteries, veins, and vessels in the macula increased risk by 9.9% to 12.1%. Each SD decrease in identified parameters of Vessel Area Density (VADa) and Vessel Skeleton Density (VSD) increased the risk of stroke by 11.6% to 19.0%

Tortuosity

Among 30 parameters extracted using 10 extraction methods, only arterial Inflection Count Tortuosity was found to be associated with stroke risk. Each SD decrease increased the risk by 10.1% (1/0.908 = 1.101).

Predictive Models for Incident Stroke Risk

A total of 73 parameters were included in the logistic regression model after removing parameters with VIF > 10 (Supplementary Table 3). When using only traditional risk factors, an AUC of 0.738 was achieved. When incorporating retinal parameters in the model, there was a statistically significant increase in the AUC, reaching 0.752 (P<0.001). In addition, when only age and sex, along with retinal parameters, were used, there was still a slight improvement in AUC (0.739), though without statistical significance.

Non-linear association, subgroup and sensitivity analyses

Among 29 identified parameters, only Number of vessel Segments in the macular region showed a non-linear association, a L-pattern with HR decreasing with increase in the Number and then levelling off when the Number reached 60. (Supplementary Figure 1) Additionally, when examined as categorical variables, arterial Asymmetry Ratio, the Number of vessel branching points in the macular region, and VSD of veins in and outside the macular region showed potential non-linear associations. (Supplementary Figure 2 and Supplementary Table 4) Furthermore, the sensitivity analyses showed 27 out of 29 remained significant associations when individuals with cardiovascular disease risk were kept and all maintained significance in the other two analyses. Supplementary Tables 5-10 show the results of subgroup analyses.

Discussion

This study represents a comprehensive exploration of retinal vascular parameters, encompassing 118 measurements across 30 distinct measure types categorized into five groups. After adjusting for traditional risk factors and multiple testing, we identified 29 indicators of increased stroke risk. Moreover, we showed that incorporating retinal parameters significantly improved incident stroke prediction. Even when only using age, sex, and retinal vascular parameters, the AUC was comparable to the performance of the model using traditional risk factors, testifying to the potential of retinal parameters for stroke risk prediction as a non-invasive tool.

Over half of the identified parameters were Density-related, highlighting the unique role of density in assessing incident stroke risk. Interestingly, increased Arc Length and Chord Length, rarely studied independently before, were associated with a higher risk of stroke, which aligns with previous research demonstrating their link to increased mortality risk[21]. Additionally, our study showed that arterial VSD and VAD across the entire fundus image, in the macula, and outside the macular region demonstrated an inverse association with incident stroke risk. This finding was consistent with previous studies[11,22] that found associations with stroke risk factors, including age, hypertension, and atherosclerosis. Our findings indicate that this association is mainly due to arterial Density parameters. Pathologically, this could result from compromised oxygen and nutrient supply[23].

Moreover, while no association between bifurcation and stroke mortality was found in a previous study[24], we found that arterial Bifurcation Density was associated with stroke risk when examining arterial and venular parameters separately. Furthermore, arterial Branching Density and Branching Density of vessels in the macula were all associated with stroke risk. Those changes may indicate impaired endothelial function, vascular bifurcation, collateral circulation, and an increased risk of hypoxia[25,26].

Retinal vascular calibre is one of the most studied parameters, and in this study, CRAE and LDR parameters were associated with stroke risk. LDR is dimensionless and free from refractive indices of optical media; thus, it was considered a more sensitive and reliable indicator[27]. Previous studies reported that increased LDRa is associated with known stroke risk factors such as hypertension[27] and high neocortical plaque burden[28]. Our study further supports that even when adjusted for stroke risk factors, LDRa was still positively associated with stroke risk.

In addition, reduced Complexity, such as reduced FD, lower Number of bifurcation, branching, and segments, and lower arterial Inflection Count Tortuosity were associated with increased stroke risk. FD reflects the complexity and irregularity of the retinal vascular pattern[22], and previous research also found a lower FD is associated with a higher risk of incident stroke[11]. We examined arterial and venular FD separately and found the association was mainly attributable to FDa. While previous studies widely studied tortuosity and stroke risk, the findings were inconclusive[8,9,24]. This might be attributed to differences in extraction methods. In our study, we used 10 different methods to generate 30 Tortuosity parameters, and only one showed significant association. This emphasizes the difficulty of elucidating the relationship between tortuosity and stroke risk. These observed changes in Complexity and Tortuosity may indicate reduced perfusion, impaired collateral circulation, increased risk of hypoxia, higher susceptibility to damage from stroke risk factors, higher prevalence of cerebral microbleeds, and impaired oxygenation [22,26,29].

Beyond identifying risk indicators, we explored the potential of those parameters in predicting stroke. Compared with the AUC achieved with traditional risk factors, the introduction of retinal parameters significantly improved the AUC from 0.738 to 0.752. This is only a small increase in AUC and likely would have little impact on screening performance. That said, when using age, sex, and retinal vascular parameters, the AUC was similar to the fully adjusted traditional model (0.739 vs. 0.738). Obtaining this estimate requires a blood draw and biochemistry tests such as cholesterol level and HbA1C, which is not needed when using fundus photos. Given that age and sex are readily available, demographic information and retinal parameters can be obtained through routine fundus photography; this model presents a practical and easily implementable approach for incident stroke risk assessment, particularly for primary health care and low-resource settings. In addition, a previous study demonstrated the cost-effectiveness of retinal fundus-based AI screening for multiple ocular diseases, particularly in primary healthcare settings[30]. We believe including stroke risk assessment in such models would further enhance their utility, offering a comprehensive, cost-effective tool for early detection and prevention of both ocular and systemic diseases, particularly in underserved or resource-limited healthcare settings.

Our study performed a comprehensive analysis of retinal vascular parameters extracted with RMHAS from a vast dataset of fundus images within the UK Biobank cohort. Additionally, we adjusted for traditional risk factors and explored their association with incident stroke using Cox proportional hazard regression and FDR method. It’s noteworthy that when examined separately as arterial and venular parameters, most parameters showing significance were arterial parameters. Additionally, more than half of the identified parameters were Density parameters. While previous studies investigated associations between retinal vascular parameters and stroke, Density parameters were rarely studied. Our study unveiled that they hold unique values as sensitive indicators. More importantly, in this study, we were able to reveal the added predictive value of parameters generated by RMHAS.

This study's observational nature limits the establishment of causality between retinal vascular parameters and stroke risk. A randomized controlled trial comparing patient outcomes using traditional risk factors alone versus a combination of traditional factors and retinal biomarkers for monitoring and managing stroke risk would help determine whether the addition of retinal vascular parameters offers a significant improvement. Furthermore, considering that about 90% of the UK Biobank cohort participants were of white ethnicity, the generalizability of the findings is limited. We also recognize that while AUC increase has statistical significance, its clinical value is limited. Adding this analysis allows for a non-invasive, cost-effective screening solution rather than a clinical tool. Additionally, since the number of incident strokes was not large, we were not able to investigate the associations by subtypes of stroke. Lastly, we used ICD collected during hospitalization to identify incident strokes. This may underestimate stroke incidence since patients with mild stroke are not necessarily hospitalized. These limitations suggest the need for caution in inferring causal relationships and highlight the necessity for further research to validate findings and explore the intricacies of retinal vascular parameters concerning stroke risk across diverse populations.

In summary, our study showed that this set of comprehensive retinal vascular parameters was of added predictive value for incident stroke, indicating its potential application as a non-invasive screening method for individuals with increased risk. After adjusting for traditional risk factors, 17 Density parameters, 8 Complexity parameters, and 3 Calibre and 1 Tortuosity parameters were significantly associated with increased stroke risk. Further investigation of these parameters may provide valuable insights into the intricate pathophysiological processes associated with stroke, thereby contributing to the refinement of preventive and therapeutic strategies.

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Disclosures:

The authors declare no conflict of interest.

Author Contributions:

Conceptualization, XS and MH; Methodology, DS, MY and XS; Analysis, MY, MK, and AP, Manuscript drafting, MY; Manuscript review & critical revision, XS, DS, DF, MK, and AP; Visualization, MY and MK; Supervision, DS, XS, LZ, and MH; Project administration, DS, XS, LZ, and MH. MY is the guarantor.

Patient and Public Involvement

In the phase 1 pilot study between February and March 2005 and an integrated pilot from March to June 2006, feedback from participants was obtained to refine the study protocol in the UK Biobank study.

Data Availability Statement

This study used data from a public, open access repository, the UK Biobank study (https://www.ukbiobank.ac.uk/).

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Table 1. Baseline demographic characteristics of participants

	All (N=45161)	Incident stroke (N=749)	Stroke-free (N=44412)	P-value
Age				<0.001
Mean (SD)	55.4 (8.18)	61.3 (6.80)	55.3 (8.17)	
Sex				<0.001
Female	24785 (54.9%)	342 (45.7%)	24443 (55.0%)	
Male	20376 (45.1%)	407 (54.3%)	19969 (45.0%)	
Ethnicity				0.39
White	41206 (91.2%)	687 (91.7%)	40519 (91.2%)	
Mixed	391 (0.9%)	3 (0.4%)	388 (0.9%)	
Asian	1387 (3.1%)	20 (2.7%)	1367 (3.1%)	
Black	1265 (2.8%)	21 (2.8%)	1244 (2.8%)	
Other	642 (1.4%)	15 (2.0%)	627 (1.4%)	
Missing	270 (0.6%)	3 (0.4%)	267 (0.6%)	
Indices of Multiple Deprivation				0.117
Mean (SD)	17.4 (12.6)	18.2 (13.2)	17.4 (12.6)	
Missing	700 (1.6%)	11 (1.5%)	689 (1.6%)	
Education				<0.001
High	17435 (38.6%)	222 (29.6%)	17213 (38.8%)	
Intermediate	22388 (49.6%)	370 (49.4%)	22018 (49.6%)	
Low	4846 (10.7%)	141 (18.8%)	4705 (10.6%)	
Missing	492 (1.1%)	16 (2.1%)	476 (1.1%)	
Body mass index				<0.001
Mean (SD)	27.1 (4.67)	28.0 (4.82)	27.1 (4.66)	
Missing	203 (0.4%)	7 (0.9%)	196 (0.4%)	
Smoking status				<0.001
Never	26250 (58.1%)	373 (49.8%)	25877 (58.3%)	
Previous	14642 (32.4%)	274 (36.6%)	14368 (32.4%)	
Current	4027 (8.9%)	96 (12.8%)	3931 (8.9%)	
Missing	242 (0.5%)	6 (0.8%)	236 (0.5%)	
Drinking status				0.609
Never	2037 (4.5%)	34 (4.5%)	2003 (4.5%)	
Previous	1458 (3.2%)	29 (3.9%)	1429 (3.2%)	
Current	41514 (91.9%)	685 (91.5%)	40829 (91.9%)	
Missing	152 (0.3%)	1 (0.1%)	151 (0.3%)	
SBP				<0.001
Mean (SD)	136 (18.1)	144 (19.9)	136 (18.0)	

	All (N=45161)	Incident stroke (N=749)	Stroke-free (N=44412)	P-value
Missing	147 (0.3%)	4 (0.5%)	143 (0.3%)	
DBP				<0.001
Mean (SD)	81.5 (10.0)	83.7 (10.6)	81.5 (10.0)	
Missing	147 (0.3%)	4 (0.5%)	143 (0.3%)	
Cholesterol				0.315
Mean (SD)	5.74 (1.10)	5.70 (1.17)	5.74 (1.10)	
Missing	3774 (8.4%)	71 (9.5%)	3703 (8.3%)	
HDL				<0.001
Mean (SD)	1.49 (0.386)	1.43 (0.385)	1.49 (0.386)	
Missing	6140 (13.6%)	106 (14.2%)	6034 (13.6%)	
LDL				0.601
Mean (SD)	3.58 (0.840)	3.56 (0.876)	3.58 (0.839)	
Missing	3854 (8.5%)	72 (9.6%)	3782 (8.5%)	
Diabetes				<0.001
No	43170 (95.6%)	673 (89.9%)	42497 (95.7%)	
Yes	1753 (3.9%)	72 (9.6%)	1681 (3.8%)	
Missing	238 (0.5%)	4 (0.5%)	234 (0.5%)	

Notes: SD: standard deviation, SBP: systolic blood pressure, DBP: diastolic blood pressure, LDL: low-density lipoprotein, HDL: high-density lipoprotein. The continuous variables were reported as mean (SD), and categorical variables were presented as count (percentage). To compare differences between groups, for continuous variables, we used either a t-test (normal distribution) or the Wilcoxon rank-sum test (for non-normal distributions), and for categorical variables, we used the chi-squared test.

Figure Legends

Figure 1. Retinal Vascular Network Segmentation and Quantification

Figure 2. Participants selection process

Figure 3. Association between retinal vascular parameters and risk of incident stroke

Notes: The Adjusted Model was adjusted for age, sex, systolic blood pressure, total cholesterol, HDL, HbA1c, smoking, BMI, and Indices of Multiple Deprivation at baseline. * The False Discovery Rate method was used to adjust P values at a level of 0.05. HDL indicates high-density lipoprotein; HbA1c, glycosylated hemoglobin; BMI, body mass index; HR, hazard ratio, and CI, Confidence Interval. HR represents the relative risk of incident stroke for each 1 standard deviation increase in the exposure. The results of the unadjusted model can be found in Supplementary Figure 4.

STROBE Statement—checklist of items that should be included in reports of observational studies.

	Item No.	Recommendation	Page No.	Line No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Title
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	2-29
Objectives	3	State specific objectives, including any prespecified hypotheses	4	30-34
Methods				
Study design	4	Present key elements of study design early in the paper	4	38
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	40-47
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5	46-47, 74-78
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6	49-80, Supplementary Table 1
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	5,6	49-80,

measurement		assessment (measurement). Describe comparability of assessment methods if there is more than one group		Supplementary Table 1
Bias	9	Describe any efforts to address potential sources of bias	6	91-100
Study size	10	Explain how the study size was arrived at	5	46-47, 77-81, Figure 2
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6	84-87
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6	84-104
		(*b*) Describe any methods used to examine subgroups and interactions	6	96-97
		(*c*) Explain how missing data were addressed	6	86-87
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	5	77-82
		(*e*) Describe any sensitivity analyses	6	93-96
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6	107-113, Figure 2
		(b) Give reasons for non-participation at each stage	6	107-113, Figure 2
		(c) Consider use of a flow diagram	Figure 2	Figure 2
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6,7, Table 1	114-120, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1	Table 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	6	114-115
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	6	115-116

		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7,8	121-171, Figure 3
		(*b*) Report category boundaries when continuous variables were categorized	8	172-178, Supplementary Figure 2 and Table 4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8	185-191, Supplementary Figures 1-3, Supplementary Tables 4-10
Discussion				
Key results	18	Summarise key results with reference to study objectives	8	184-192
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10,11	260-276
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9,10	193-259
Generalisability	21	Discuss the generalisability (external validity) of the study results	10	265-266
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11	287-294

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Supplementary Table 1. Definition of variables from UK Biobank study

Variable	**Definition and collection**	**Link**
Age	Age when attended assessment centre	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=21003
Sex	Sex of participant. Acquired from central registry at recruitment, but in some cases updated by the participant. Hence this field may contain a mixture of the sex the NHS had recorded for the participant and self-reported sex.	http://biobank.ndph.ox.ac.uk/ukb/field.cgi?id=31
Indices of Multiple Deprivaton	Indices of Multiple Deprivation come from a UK government qualitative study of deprived areas in British local councils. The study is conducted separately in England (IMD), Scotland (SIMD) and Wales (WIMD). Scores were gathered from open data published by the UK government.	https://biobank.ndph.ox.ac.uk/showcase/label.cgi?id=76
Body mass index (BMI)	Defined as weight in kilogrammes divided by height in metres squared. BMI value here is constructed from height and weight measured during the initial Assessment Centre visit. Value is not present if either of these readings were omitted.	http://biobank.ndph.ox.ac.uk/ukb/field.cgi?id=21001
glycosylated hemoglobin	Measured by HPLC analysis on a Bio-Rad VARIANT II Turbo	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=30750
Diabetes	ACE touchscreen question \Has a doctor ever told you that you have diabetes?\" If the participant activated the Help button they were shown the message: If you are unsure if you have been told you had diabetes select Do not know and you will be asked about this by an interviewer later during this visit. "	http://biobank.ndph.ox.ac.uk/ukb/field.cgi?id=2443
Smoking status	This field summarises the current/past smoking status of the participant. Current/Previous/Never used in Cox regression	http://biobank.ndph.ox.ac.uk/ukb/field.cgi?id=20116
Systolic Blood Pressure	Blood pressure, automated reading, systolic. Omron device. Units of measurement are mmHg.	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=4080

Diastolic Blood Pressure	Blood pressure, automated reading, diastolic. Omron device. Units of measurement are mmHg.	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=4079
Low-Density Lipoprotein	Measured by enzyme immunoinhibition analysis on a Beckman Coulter AU5800. Units of measurement are mmol/L.	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=30780
High-Density Lipoprotein	Measured by enzyme immunoinhibition analysis on a Beckman Coulter AU5800. Units of measurement are mmol/L.	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=30760
Cholesterol	Measured by Choline (CHO) - Pseudocholinesterase (POD) analysis on a Beckman Coulter AU5800	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=30690
Cancer	ACE touchscreen question \Has a doctor ever told you that you have had cancer?\" If the participant activated the Help button they were shown the message: If you are unsure if you have been told you had cancer select Do not know and you will be asked about this by an interviewer later during this visit. "	http://biobank.ndph.ox.ac.uk/ukb/field.cgi?id=2453
Stroke	Prior record of event was determined using answers from Field ID 6150 and data coding "1081, 1086, 1491, 1583" from Field ID 20002. In addition, if record of event was earlier than the time attending accessment center, the event was considered prior event as well using ICD-10 "I600", "I601", "I602", "I603", "I604", "I605", "I606", "I607", "I608", "I609", "I610", "I611", "I612", "I613", "I614", "I615", "I616", "I618", "I619", "I630", "I631", "I632", "I633", "I634", "I635", "I636", "I638", "I639", "I64", "I679", "I694" from data field ID 41289 and 41270 and ICD-9 "4309", "4319", "4349", "4369" from data field ID 41281 and 41271	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=6150

Heart attack	ACE touchscreen question "Has a doctor ever told you that you have had any of the following conditions? (You can select more than one answer)" The following checks were performed: If code -7 was selected, then no additional choices were allowed. If code -3 was selected, then no additional choices were allowed. If the participant activated the Help button they were shown the message: f you do not know if you have had any of the listed conditions, enter None of the above. You can check this with an interviewer later in the visit.	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=6150
Heart Failure	Prior record of event was determinded using data coding "1076" from Field ID 20002.	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=20002
Peripheral Vascular Disease	Prior record of event was determinded using data coding "1081, 1086, 1491, 1583" from Field ID 20002.	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=20002
Myocardial infarction	Prior record of event was determinded using data coding "1075" from Field ID 20002.	https://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=20002

Supplementary Table 2. Included and excluded participants with eligible image

	All (N=51390)	Excluded (N=6229)	Included (N=45161)	P-value
Age				
Mean (SD)	55.9 (8.22)	60.0 (7.26)	55.4 (8.18)	<0.001
Sex				
Female	28129 (54.7%)	3344 (53.7%)	24785 (54.9%)	0.0774
Male	23261 (45.3%)	2885 (46.3%)	20376 (45.1%)	
Ethnicity				
White	47094 (91.6%)	5888 (94.5%)	41206 (91.2%)	<0.001
Mixed	426 (0.8%)	35 (0.6%)	391 (0.9%)	
Asian	1514 (2.9%)	127 (2.0%)	1387 (3.1%)	
Black	1361 (2.6%)	96 (1.5%)	1265 (2.8%)	
Other	699 (1.4%)	57 (0.9%)	642 (1.4%)	
Missing	296 (0.6%)	26 (0.4%)	270 (0.6%)	
Indices of Multiple Deprivation				
Mean (SD)	17.5 (12.7)	17.9 (13.2)	17.4 (12.6)	0.0183
Missing	819 (1.6%)	119 (1.9%)	700 (1.6%)	
Education				
High	19484 (37.9%)	2049 (32.9%)	17435 (38.6%)	<0.001
Intermediate	25370 (49.4%)	2982 (47.9%)	22388 (49.6%)	
Low	5971 (11.6%)	1125 (18.1%)	4846 (10.7%)	
Missing	565 (1.1%)	73 (1.2%)	492 (1.1%)	
Body mass index				
N	51157	6199	44958	<0.001
Mean (SD)	27.1 (4.70)	27.7 (4.93)	27.1 (4.67)	
Median [Min, Max]	26.5 [12.6, 66.0]	27.0 [16.6, 56.2]	26.4 [12.6, 66.0]	
IQR	5.63	6.09	5.57	
Missing	233 (0.5%)	30 (0.5%)	203 (0.4%)	
Smoking status				
Never	29385 (57.2%)	3135 (50.3%)	26250 (58.1%)	<0.001
Previous	17150 (33.4%)	2508 (40.3%)	14642 (32.4%)	
Current	4587 (8.9%)	560 (9.0%)	4027 (8.9%)	
Missing	268 (0.5%)	26 (0.4%)	242 (0.5%)	
Drinking status				

	All (N=51390)	Excluded (N=6229)	Included (N=45161)	P-value
Never	2323 (4.5%)	286 (4.6%)	2037 (4.5%)	<0.001
Previous	1748 (3.4%)	290 (4.7%)	1458 (3.2%)	
Current	47157 (91.8%)	5643 (90.6%)	41514 (91.9%)	
Missing	162 (0.3%)	10 (0.2%)	152 (0.3%)	
Systolic Blood Pressure				
Mean (SD)	136 (18.1)	137 (18.3)	136 (18.1)	<0.001
Missing	172 (0.3%)	25 (0.4%)	147 (0.3%)	
Diastolic Blood Pressure				
Mean (SD)	81.4 (10.0)	80.5 (9.84)	81.5 (10.0)	<0.001
Missing	172 (0.3%)	25 (0.4%)	147 (0.3%)	
Cholesterol				
Mean (SD)	5.70 (1.13)	5.37 (1.27)	5.74 (1.10)	<0.001
Missing	4427 (8.6%)	653 (10.5%)	3774 (8.4%)	
High-Density Lipoprotein				
Mean (SD)	1.49 (0.388)	1.44 (0.401)	1.49 (0.386)	<0.001
Missing	7091 (13.8%)	951 (15.3%)	6140 (13.6%)	
Low-Density Lipoprotein				
Mean (SD)	3.55 (0.857)	3.30 (0.940)	3.58 (0.840)	<0.001
Missing	4520 (8.8%)	666 (10.7%)	3854 (8.5%)	
Diabetes				
No	48833 (95.0%)	5663 (90.9%)	43170 (95.6%)	<0.001
Yes	2283 (4.4%)	530 (8.5%)	1753 (3.9%)	
Missing	274 (0.5%)	36 (0.6%)	238 (0.5%)	

Notes: SD: standard deviation. The continuous variables were reported as mean (SD), and categorical variables were presented as count (percentage). To compare differences between groups, for continuous variables, we used either a t-test (normal distribution) or the Wilcoxon rank-sum test (for non-normal distributions), and for categorical variables, we used the chi-squared test.

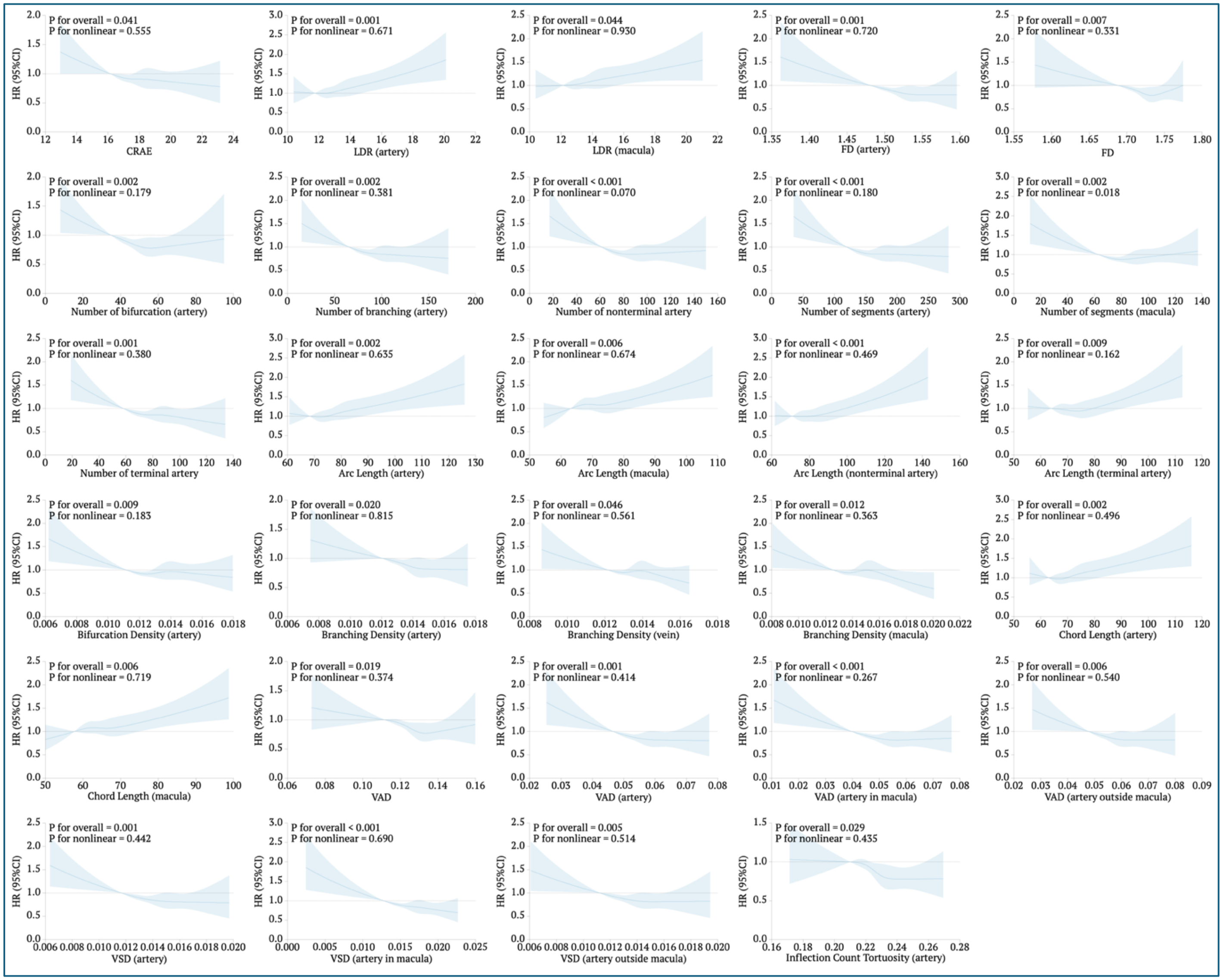
Supplementary Table 3. RMHAS-generated parameters with acceptable variance inflation factor (<10)

Category	**Measure type**	**Parameter**
Branching Angle	Angular Asymmetry	Angular Asymmetry(edge)(artery)
Branching Angle	Angular Asymmetry	Angular Asymmetry(edge)(vein)
Branching Angle	Angular Asymmetry	Angular Asymmetry(edge)-macula
Branching Angle	Angular Asymmetry	Angular Asymmetry(artery)
Branching Angle	Angular Asymmetry	Angular Asymmetry(vein)
Branching Angle	Angular Asymmetry	Angular Asymmetry-macula
Branching Angle	Asymmetry Ratio	Asymmetry Ratio(artery)
Branching Angle	Asymmetry Ratio	Asymmetry Ratio(vein)
Branching Angle	Asymmetry Ratio	Asymmetry Ratio-macula
Branching Angle	Branching Angle	Branching Angle(edge)(artery)
Branching Angle	Branching Angle	Branching Angle(edge)(vein)
Branching Angle	Branching Angle	Branching Angle(edge)-macula
Branching Angle	Branching Angle	Branching Angle(artery)
Branching Angle	Branching Angle	Branching Angle(vein)
Branching Angle	Branching Angle	Branching Angle-macula
Branching Angle	Branching Coefficient	Branching Coefficient(artery)
Branching Angle	Branching Coefficient	Branching Coefficient(vein)
Branching Angle	Branching Coefficient	Branching Coefficient-macula
Branching Angle	Junctional Exponent Deviation	Junctional Exponent Deviation(artery)
Branching Angle	Junctional Exponent Deviation	Junctional Exponent Deviation(vein)
Branching Angle	Junctional Exponent Deviation	Junctional Exponent Deviation-macula

Calibre	Artery-to-Vein Ratio	Artery-to-Vein Ratio (from equivalents)
Calibre	Central Retinal Artery Equivalent	Central Retinal Artery Equivalent
Calibre	Central Retinal Vein Equivalent	Central Retinal Vein Equivalent
Calibre	Width	Calibre-macula
Complexity	Level	level(artery)
Complexity	Level	level(vein)
Complexity	Level	level-macula
Complexity	Number	Number of vessel tree(artery)
Complexity	Number	Number of vessel tree(vein)
Complexity	Number	Number of vessel tree-macula
Complexity	Strahler	Strahler(artery)
Complexity	Strahler	Strahler(vein)
Complexity	Strahler	Strahler-macula
Density	Bifurcation Density	Bifurcation density(artery)
Density	Bifurcation Density	Bifurcation density(vein)
Density	Bifurcation Density	Bifurcation density-macula
Density	Branching Density	Branching density(artery)
Density	Branching Density	Branching density(vein)
Density	Branching Density	Branching density-macula
Density	Vessel Area Density	Vessel Area Density(vein)-macula
Density	Vessel Skeleton Density	Vessel Skeleton Density(artery)-macula
Density	Vessel Skeleton Density	Vessel Skeleton Density(vein)-macula
Tortuosity	Turning Angles	Turning angles(artery)
Tortuosity	Turning Angles	Turning angles(vein)
Tortuosity	Turning Angles	Turning angles-macula
Tortuosity	Angle-based Tortuosity	Angle-based tortuosity(artery)
Tortuosity	Angle-based Tortuosity	Angle-based tortuosity(vein)
Tortuosity	Angle-based Tortuosity	Angle-based tortuosity-macula
Tortuosity	Curve Angle	Curve Angle(artery)
Tortuosity	Curve Angle	Curve Angle(vein)
Tortuosity	Curve Angle	Curve Angle-macula
Tortuosity	Squared Curvature Tortuosity	Squared curvature tortuosity(artery)
Tortuosity	Squared Curvature Tortuosity	Squared curvature tortuosity(vein)
Tortuosity	Squared Curvature Tortuosity	Squared curvature tortuosity-macula
Tortuosity	Fractal Tortuosity	Fractal tortuosity(artery)
Tortuosity	Fractal Tortuosity	Fractal tortuosity(vein)
Tortuosity	Fractal Tortuosity	Fractal tortuosity-macula

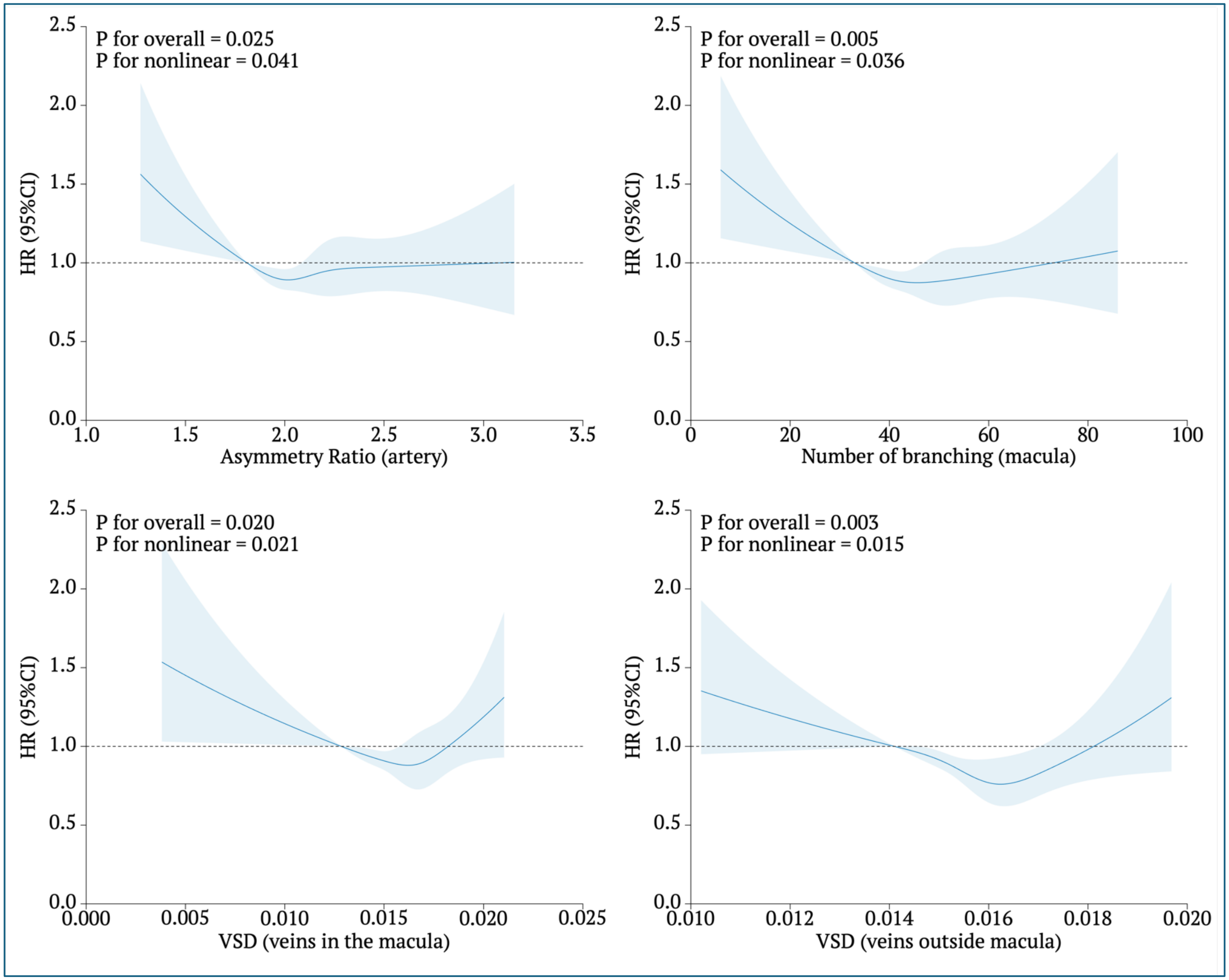
Tortuosity	Inflection Count Tortuosity	Inflection count tortuosity(artery)
Tortuosity	Inflection Count Tortuosity	Inflection count tortuosity(vein)
Tortuosity	Inflection Count Tortuosity	Inflection count tortuosity-macula
Tortuosity	Linear Regression Tortuosity	Linear regression tortuosity(artery)
Tortuosity	Linear Regression Tortuosity	Linear regression tortuosity(vein)
Tortuosity	Linear Regression Tortuosity	Linear regression tortuosity-macula
Tortuosity	Tortuosity Density	Tortuosity Density(artery)
Tortuosity	Tortuosity Density	Tortuosity Density(vein)
Tortuosity	Tortuosity Density	Tortuosity Density-macula
Tortuosity	Distance-based Tortuosity	Distance-based tortuosity(artery)
Tortuosity	Distance-based Tortuosity	Distance-based tortuosity(vein)
Tortuosity	Distance-based Tortuosity	Distance-based tortuosity-macula
Tortuosity	Twist-based Tortuosity	Twist-based tortuosity(artery)
Tortuosity	Twist-based Tortuosity	Twist-based tortuosity(vein)
Tortuosity	Twist-based Tortuosity	Twist-based tortuosity-macula

Supplementary Figure 1. Restricted Cubic Spline for retinal vascular parameters with linear association with incident stroke risk



Data were fitted by a restricted cubic spline Cox proportional hazards regression model, and the model was conducted with 4 knots at the 20th, 40th, 60th, 80th percentiles. Model was adjusted for age, sex, systolic blood pressure, total cholesterol, HDL, HbA1c, smoking, BMI, and Indices of Multiple Deprivation at baseline. HDL indicates high-density lipoprotein; HbA1c, glycosylated hemoglobin; BMI, body mass index; CRAE, Central Retinal Artery Equivalent; LDR, Length-to-Diameter Ratio; FD, Fractal Dimension; VAD, Vessel Area Density, VSD, Vessel Skeleton Density; HR, hazard ratio, and CI, Confidence Interval.

Supplementary Figure 2. Non-linear associations between retinal vascular parameters and incident stroke risk



Data were fitted by a restricted cubic spline Cox proportional hazards regression model, and the model was conducted with 4 knots at the 20th, 40th, 60th, 80th percentiles. Model was adjusted for age, sex, systolic blood pressure, total cholesterol, HDL, HbA1c, smoking, BMI, and Indices of Multiple Deprivation at baseline. HDL indicates high-density lipoprotein; HbA1c, glycosylated hemoglobin; BMI, body mass index; HR, hazard ratio, VSD, Vessel Skeleton Density; and CI, Confidence Interval.

Supplementary Table 4. Non-linear associations between retinal vascular parameters as quintiles and incident stroke risk

Parameters	**Quintile**	**Unadjusted model HR (95%CI)**	**FDR-adjusted P value**	**Adjusted model HR (95%CI)**	**–FDR-adjusted P value**
Angular Asymmetry (edge) (artery)	Q2	0.839 (0.673 - 1.048)	0.191933	0.975 (0.781 - 1.217)	0.93115
Angular Asymmetry (edge) (artery)	Q3	0.819 (0.655 - 1.023)	0.13244	0.980 (0.784 - 1.225)	0.940649
Angular Asymmetry (edge) (artery)	Q4	0.814 (0.651 - 1.018)	0.122385	0.999 (0.798 - 1.250)	0.998115
Angular Asymmetry (edge) (artery)	Q5	0.873 (0.701 - 1.087)	0.313389	1.030 (0.827 - 1.284)	0.918306
Angular Asymmetry (edge) (vein)	Q2	0.748 (0.598 - 0.936)	0.023897	0.852 (0.681 - 1.067)	0.409165
Angular Asymmetry (edge) (vein)	Q3	0.761 (0.609 - 0.951)	0.033606	0.883 (0.706 - 1.105)	0.551964
Angular Asymmetry (edge) (vein)	Q4	0.847 (0.682 - 1.052)	0.206101	1.014 (0.816 - 1.260)	0.963637
Angular Asymmetry (edge) (vein)	Q5	0.820 (0.659 - 1.020)	0.127275	0.999 (0.802 - 1.243)	0.998115
Angular Asymmetry (edge)-macula	Q2	0.937 (0.744 - 1.181)	0.66647	0.998 (0.792 - 1.258)	0.998115
Angular Asymmetry (edge)-macula	Q3	1.025 (0.817 - 1.285)	0.86788	1.090 (0.869 - 1.367)	0.698831
Angular Asymmetry (edge)-macula	Q4	0.953 (0.756 - 1.200)	0.749109	1.009 (0.801 - 1.270)	0.988723
Angular Asymmetry (edge)-macula	Q5	1.150 (0.922 - 1.434)	0.303427	1.102 (0.884 - 1.374)	0.647027
Angular Asymmetry (artery)	Q2	0.826 (0.666 - 1.025)	0.137056	0.963 (0.776 - 1.195)	0.893228
Angular Asymmetry (artery)	Q3	0.731 (0.586 - 0.914)	0.013784	0.922 (0.737 - 1.152)	0.710159
Angular Asymmetry (artery)	Q4	0.827 (0.667 - 1.025)	0.138779	1.041 (0.839 - 1.292)	0.88739
Angular Asymmetry (artery)	Q5	0.668 (0.532 - 0.839)	0.001469	0.844 (0.671 - 1.061)	0.383891
Angular Asymmetry (vein)	Q2	0.929 (0.746 - 1.157)	0.598691	1.043 (0.837 - 1.299)	0.881835
Angular Asymmetry (vein)	Q3	0.825 (0.658 - 1.033)	0.153763	0.990 (0.789 - 1.241)	0.983246
Angular Asymmetry (vein)	Q4	0.841 (0.672 - 1.053)	0.204908	1.050 (0.839 - 1.315)	0.85554
Angular Asymmetry (vein)	Q5	0.869 (0.696 - 1.085)	0.303427	1.127 (0.902 - 1.409)	0.560679
Angular Asymmetry-macula	Q2	1.047 (0.836 - 1.312)	0.754925	1.145 (0.914 - 1.435)	0.504858
Angular Asymmetry-macula	Q3	0.941 (0.747 - 1.187)	0.689547	1.070 (0.848 - 1.348)	0.786314
Angular Asymmetry-macula	Q4	0.893 (0.706 - 1.128)	0.43916	0.997 (0.789 - 1.261)	0.998115
Angular Asymmetry-macula	Q5	1.176 (0.944 - 1.465)	0.226679	1.244 (0.999 - 1.550)	0.242545
Turning angles (artery)	Q2	0.921 (0.733 - 1.157)	0.571614	0.995 (0.792 - 1.250)	0.996454

Turning angles (artery)	Q3	0.828 (0.655 - 1.047)	0.182336	0.882 (0.697 - 1.116)	0.560679
Turning angles (artery)	Q4	0.969 (0.774 - 1.214)	0.831508	1.037 (0.828 - 1.300)	0.900076
Turning angles (artery)	Q5	1.152 (0.928 - 1.431)	0.285241	1.108 (0.892 - 1.376)	0.616401
Turning angles (vein)	Q2	1.091 (0.865 - 1.375)	0.556733	1.120 (0.888 - 1.412)	0.600318
Turning angles (vein)	Q3	1.107 (0.879 - 1.395)	0.484693	1.125 (0.893 - 1.418)	0.58276
Turning angles (vein)	Q4	1.135 (0.902 - 1.428)	0.375633	1.166 (0.927 - 1.467)	0.440716
Turning angles (vein)	Q5	1.128 (0.896 - 1.420)	0.403322	1.097 (0.871 - 1.381)	0.681444
Turning angles-macula	Q2	1.232 (0.980 - 1.548)	0.126526	1.285 (1.022 - 1.615)	0.185478
Turning angles-macula	Q3	0.986 (0.775 - 1.255)	0.933684	1.031 (0.810 - 1.312)	0.924628
Turning angles-macula	Q4	1.140 (0.903 - 1.438)	0.367199	1.169 (0.926 - 1.475)	0.440716
Turning angles-macula	Q5	1.264 (1.007 - 1.586)	0.080744	1.245 (0.991 - 1.563)	0.249966
Angle-based tortuosity (artery)	Q2	1.077 (0.858 - 1.353)	0.605986	1.151 (0.917 - 1.446)	0.498685
Angle-based tortuosity (artery)	Q3	1.075 (0.856 - 1.350)	0.619403	1.141 (0.909 - 1.433)	0.522677
Angle-based tortuosity (artery)	Q4	0.910 (0.718 - 1.154)	0.535689	0.970 (0.765 - 1.230)	0.924628
Angle-based tortuosity (artery)	Q5	1.141 (0.912 - 1.428)	0.341834	1.148 (0.917 - 1.437)	0.500907
Angle-based tortuosity (vein)	Q2	0.992 (0.796 - 1.236)	0.960466	1.033 (0.829 - 1.286)	0.911634
Angle-based tortuosity (vein)	Q3	0.812 (0.644 - 1.023)	0.132131	0.860 (0.682 - 1.084)	0.465351
Angle-based tortuosity (vein)	Q4	0.968 (0.776 - 1.207)	0.821414	1.008 (0.808 - 1.257)	0.990857
Angle-based tortuosity (vein)	Q5	0.893 (0.713 - 1.119)	0.423979	0.886 (0.707 - 1.110)	0.560679
Angle-based tortuosity-macula	Q2	0.952 (0.760 - 1.193)	0.742843	1.022 (0.816 - 1.281)	0.935829
Angle-based tortuosity-macula	Q3	0.825 (0.653 - 1.042)	0.171183	0.887 (0.702 - 1.121)	0.581933
Angle-based tortuosity-macula	Q4	1.038 (0.832 - 1.294)	0.797471	1.081 (0.867 - 1.348)	0.721307
Angle-based tortuosity-macula	Q5	1.003 (0.803 - 1.253)	0.987132	1.017 (0.814 - 1.271)	0.951062
Asymmetry Ratio (artery)	Q2	0.735 (0.591 - 0.915)	0.013784	0.809 (0.650 - 1.007)	0.249966
Asymmetry Ratio (artery)	Q3	0.758 (0.610 - 0.941)	0.025174	0.858 (0.690 - 1.066)	0.412995
Asymmetry Ratio (artery)	Q4	0.681 (0.545 - 0.851)	0.001964	0.798 (0.638 - 0.999)	0.234318
Asymmetry Ratio (artery)	Q5	0.757 (0.610 - 0.940)	0.02475	0.869 (0.699 - 1.080)	0.465351
Asymmetry Ratio (vein)	Q2	1.042 (0.824 - 1.316)	0.788008	1.082 (0.856 - 1.367)	0.744752
Asymmetry Ratio (vein)	Q3	1.178 (0.938 - 1.478)	0.23932	1.220 (0.972 - 1.531)	0.294988
Asymmetry Ratio (vein)	Q4	1.086 (0.862 - 1.368)	0.573293	1.093 (0.867 - 1.378)	0.695577

Asymmetry Ratio (vein)	Q5	1.107 (0.879 - 1.393)	0.484723	1.064 (0.845 - 1.340)	0.808408
Asymmetry Ratio-macula	Q2	0.922 (0.736 - 1.155)	0.571614	0.958 (0.764 - 1.200)	0.881835
Asymmetry Ratio-macula	Q3	0.932 (0.744 - 1.167)	0.62479	0.990 (0.791 - 1.240)	0.983246
Asymmetry Ratio-macula	Q4	0.892 (0.711 - 1.120)	0.423979	0.935 (0.744 - 1.173)	0.780866
Asymmetry Ratio-macula	Q5	1.014 (0.814 - 1.265)	0.923904	0.983 (0.788 - 1.226)	0.950307
Arc length (artery)	Q2	1.328 (0.995 - 1.774)	0.096137	0.963 (0.719 - 1.288)	0.924628
Arc length (artery)	Q3	1.629 (1.233 - 2.151)	0.001604	0.931 (0.701 - 1.237)	0.82829
Arc length (artery)	Q4	2.316 (1.781 - 3.011)	2.44E-09	1.076 (0.819 - 1.414)	0.808841
Arc length (artery)	Q5	3.421 (2.664 - 4.392)	2.03E-20	1.319 (1.011 - 1.721)	0.216741
Arc length (vein)	Q2	1.192 (0.915 - 1.551)	0.278969	0.998 (0.766 - 1.302)	0.998115
Arc length (vein)	Q3	1.476 (1.146 - 1.901)	0.006404	1.066 (0.825 - 1.376)	0.82829
Arc length (vein)	Q4	1.492 (1.159 - 1.921)	0.004889	0.931 (0.719 - 1.206)	0.805539
Arc length (vein)	Q5	2.474 (1.961 - 3.121)	3E-13	1.246 (0.978 - 1.588)	0.290385
Arc length-macula	Q2	1.447 (1.112 - 1.883)	0.013876	1.253 (0.963 - 1.631)	0.30748
Arc length-macula	Q3	1.538 (1.186 - 1.995)	0.003066	1.223 (0.941 - 1.588)	0.365375
Arc length-macula	Q4	1.731 (1.341 - 2.234)	8.3E-05	1.275 (0.986 - 1.648)	0.257525
Arc length-macula	Q5	2.414 (1.896 - 3.075)	8.77E-12	1.461 (1.143 - 1.869)	0.056363
Arc length_nonterminal (artery)	Q2	1.462 (1.097 - 1.948)	0.020758	1.089 (0.816 - 1.453)	0.781509
Arc length_nonterminal (artery)	Q3	1.797 (1.363 - 2.370)	0.000106	1.079 (0.815 - 1.430)	0.808408
Arc length_nonterminal (artery)	Q4	2.060 (1.571 - 2.701)	7.81E-07	1.000 (0.756 - 1.323)	0.998115
Arc length_nonterminal (artery)	Q5	3.603 (2.801 - 4.633)	1.02E-21	1.435 (1.099 - 1.873)	0.083163
Arc length_nonterminal (vein)	Q2	1.023 (0.787 - 1.328)	0.897786	0.853 (0.656 - 1.108)	0.503569
Arc length_nonterminal (vein)	Q3	1.298 (1.013 - 1.662)	0.07356	0.949 (0.739 - 1.219)	0.869815
Arc length_nonterminal (vein)	Q4	1.438 (1.128 - 1.835)	0.008434	0.906 (0.707 - 1.161)	0.681444
Arc length_nonterminal (vein)	Q5	2.181 (1.740 - 2.735)	1.07E-10	1.121 (0.886 - 1.419)	0.604218
Arc length_terminal (artery)	Q2	1.194 (0.914 - 1.561)	0.278969	0.971 (0.742 - 1.269)	0.931803
Arc length_terminal (artery)	Q3	1.395 (1.077 - 1.807)	0.02475	0.973 (0.750 - 1.264)	0.932262
Arc length_terminal (artery)	Q4	1.802 (1.407 - 2.307)	1.19E-05	1.059 (0.824 - 1.361)	0.84787
Arc length_terminal (artery)	Q5	2.411 (1.904 - 3.055)	3.14E-12	1.146 (0.898 - 1.464)	0.547626
Arc length_terminal (vein)	Q2	1.065 (0.827 - 1.373)	0.704145	0.973 (0.755 - 1.254)	0.932258

Arc length_terminal (vein)	Q3	1.368 (1.076 - 1.740)	0.022789	1.136 (0.893 - 1.446)	0.562385
Arc length_terminal (vein)	Q4	1.320 (1.036 - 1.683)	0.049493	0.970 (0.760 - 1.239)	0.925639
Arc length_terminal (vein)	Q5	1.856 (1.478 - 2.331)	4.82E-07	1.112 (0.881 - 1.403)	0.633239
AVRe	Q2	0.689 (0.557 - 0.853)	0.001683	0.757 (0.611 - 0.937)	0.091797
AVRe	Q3	0.708 (0.573 - 0.875)	0.003514	0.827 (0.669 - 1.023)	0.294139
AVRe	Q4	0.609 (0.488 - 0.760)	3.96E-05	0.759 (0.608 - 0.949)	0.125307
AVRe	Q5	0.600 (0.481 - 0.749)	2.37E-05	0.820 (0.656 - 1.026)	0.294988
Branching Angle (edge) (artery)	Q2	0.905 (0.732 - 1.119)	0.459163	1.085 (0.877 - 1.342)	0.696941
Branching Angle (edge) (artery)	Q3	0.752 (0.602 - 0.939)	0.024935	0.973 (0.778 - 1.216)	0.925639
Branching Angle (edge) (artery)	Q4	0.782 (0.628 - 0.975)	0.056342	1.051 (0.843 - 1.311)	0.84787
Branching Angle (edge) (artery)	Q5	0.681 (0.542 - 0.856)	0.002564	0.914 (0.727 - 1.151)	0.691418
Branching Angle (edge) (vein)	Q2	1.008 (0.807 - 1.259)	0.960466	1.092 (0.874 - 1.364)	0.683994
Branching Angle (edge) (vein)	Q3	0.837 (0.663 - 1.056)	0.207656	0.959 (0.759 - 1.211)	0.89149
Branching Angle (edge) (vein)	Q4	0.929 (0.740 - 1.164)	0.605986	1.073 (0.856 - 1.346)	0.763564
Branching Angle (edge) (vein)	Q5	1.025 (0.822 - 1.278)	0.866517	1.119 (0.897 - 1.396)	0.5842
Branching Angle (edge)-macula	Q2	0.868 (0.689 - 1.092)	0.313389	0.942 (0.748 - 1.187)	0.822956
Branching Angle (edge)-macula	Q3	0.950 (0.759 - 1.190)	0.731311	1.065 (0.850 - 1.334)	0.801058
Branching Angle (edge)-macula	Q4	0.901 (0.717 - 1.132)	0.469044	0.991 (0.789 - 1.245)	0.986871
Branching Angle (edge)-macula	Q5	1.082 (0.870 - 1.346)	0.571614	1.102 (0.885 - 1.371)	0.647027
Branching Angle (artery)	Q2	1.038 (0.838 - 1.286)	0.788008	1.180 (0.952 - 1.462)	0.365375
Branching Angle (artery)	Q3	0.821 (0.654 - 1.031)	0.148411	1.001 (0.797 - 1.257)	0.998115
Branching Angle (artery)	Q4	0.859 (0.687 - 1.075)	0.269269	1.070 (0.854 - 1.339)	0.780866
Branching Angle (artery)	Q5	0.793 (0.631 - 0.998)	0.086525	0.990 (0.786 - 1.245)	0.983246
Branching Angle (vein)	Q2	1.029 (0.814 - 1.300)	0.85229	1.041 (0.824 - 1.315)	0.893228
Branching Angle (vein)	Q3	1.097 (0.872 - 1.381)	0.530693	1.106 (0.879 - 1.393)	0.647027
Branching Angle (vein)	Q4	1.091 (0.866 - 1.373)	0.556415	1.076 (0.855 - 1.355)	0.759236
Branching Angle (vein)	Q5	1.168 (0.931 - 1.466)	0.264367	1.043 (0.831 - 1.309)	0.88739
Branching Angle-macula	Q2	1.094 (0.867 - 1.379)	0.54693	1.130 (0.896 - 1.426)	0.562385
Branching Angle-macula	Q3	0.931 (0.731 - 1.185)	0.646	0.974 (0.765 - 1.240)	0.932258
Branching Angle-macula	Q4	1.192 (0.949 - 1.496)	0.204908	1.197 (0.953 - 1.503)	0.356868

Branching Angle-macula	Q5	1.261 (1.007 - 1.580)	0.079531	1.169 (0.934 - 1.465)	0.420452
Branching Coefficient (artery)	Q2	0.850 (0.676 - 1.070)	0.247553	0.875 (0.695 - 1.102)	0.524638
Branching Coefficient (artery)	Q3	0.896 (0.714 - 1.124)	0.43916	0.927 (0.738 - 1.163)	0.744752
Branching Coefficient (artery)	Q4	0.958 (0.767 - 1.197)	0.772328	0.974 (0.780 - 1.218)	0.93115
Branching Coefficient (artery)	Q5	1.016 (0.816 - 1.266)	0.91372	1.043 (0.837 - 1.300)	0.881835
Branching Coefficient (vein)	Q2	0.724 (0.580 - 0.904)	0.010401	0.824 (0.660 - 1.029)	0.294988
Branching Coefficient (vein)	Q3	0.737 (0.592 - 0.919)	0.015583	0.854 (0.685 - 1.066)	0.409165
Branching Coefficient (vein)	Q4	0.715 (0.572 - 0.893)	0.007561	0.804 (0.644 - 1.005)	0.249966
Branching Coefficient (vein)	Q5	0.842 (0.681 - 1.041)	0.179777	0.898 (0.726 - 1.110)	0.5842
Branching Coefficient-macula	Q2	0.833 (0.661 - 1.051)	0.195194	0.903 (0.715 - 1.139)	0.647027
Branching Coefficient-macula	Q3	0.885 (0.704 - 1.112)	0.391822	0.955 (0.760 - 1.201)	0.879586
Branching Coefficient-macula	Q4	0.908 (0.723 - 1.140)	0.50344	0.946 (0.753 - 1.188)	0.830097
Branching Coefficient-macula	Q5	1.163 (0.939 - 1.441)	0.247442	1.131 (0.912 - 1.401)	0.531479
Bifurcation density (artery)	Q2	0.648 (0.530 - 0.791)	6.92E-05	0.790 (0.646 - 0.965)	0.154948
Bifurcation density (artery)	Q3	0.502 (0.405 - 0.622)	2.32E-09	0.720 (0.579 - 0.895)	0.062531
Bifurcation density (artery)	Q4	0.504 (0.407 - 0.624)	2.34E-09	0.859 (0.690 - 1.069)	0.420452
Bifurcation density (artery)	Q5	0.362 (0.285 - 0.460)	1.74E-15	0.748 (0.584 - 0.958)	0.154948
Bifurcation density (vein)	Q2	0.736 (0.598 - 0.907)	0.00967	0.861 (0.698 - 1.061)	0.403477
Bifurcation density (vein)	Q3	0.631 (0.508 - 0.785)	0.000114	0.828 (0.665 - 1.031)	0.304928
Bifurcation density (vein)	Q4	0.603 (0.483 - 0.751)	2.4E-05	0.888 (0.711 - 1.109)	0.560679
Bifurcation density (vein)	Q5	0.589 (0.472 - 0.735)	1.11E-05	0.929 (0.741 - 1.165)	0.754709
Bifurcation density-macula	Q2	0.815 (0.661 - 1.006)	0.098688	0.959 (0.777 - 1.184)	0.879586
Bifurcation density-macula	Q3	0.612 (0.487 - 0.768)	7.45E-05	0.745 (0.593 - 0.935)	0.094692
Bifurcation density-macula	Q4	0.694 (0.557 - 0.864)	0.002806	0.897 (0.720 - 1.118)	0.598487
Bifurcation density-macula	Q5	0.705 (0.567 - 0.876)	0.004185	0.949 (0.763 - 1.182)	0.83899
Branching density (artery)	Q2	0.809 (0.668 - 0.980)	0.059738	0.983 (0.811 - 1.191)	0.940649
Branching density (artery)	Q3	0.561 (0.453 - 0.694)	4.54E-07	0.827 (0.667 - 1.026)	0.294988
Branching density (artery)	Q4	0.434 (0.345 - 0.548)	1.51E-11	0.762 (0.601 - 0.966)	0.167598
Branching density (artery)	Q5	0.360 (0.281 - 0.460)	6.34E-15	0.800 (0.620 - 1.033)	0.294988
Branching density (vein)	Q2	0.691 (0.563 - 0.849)	0.001219	0.848 (0.690 - 1.042)	0.349236

Branching density (vein)	Q3	0.703 (0.573 - 0.862)	0.001924	0.979 (0.796 - 1.203)	0.932258
Branching density (vein)	Q4	0.507 (0.405 - 0.634)	1.55E-08	0.805 (0.640 - 1.011)	0.252848
Branching density (vein)	Q5	0.430 (0.339 - 0.545)	2.62E-11	0.769 (0.603 - 0.981)	0.192991
Branching density-macula	Q2	0.652 (0.529 - 0.803)	0.000179	0.758 (0.615 - 0.935)	0.088811
Branching density-macula	Q3	0.585 (0.472 - 0.726)	4.61E-06	0.745 (0.600 - 0.926)	0.083163
Branching density-macula	Q4	0.652 (0.530 - 0.803)	0.00018	0.892 (0.723 - 1.100)	0.560679
Branching density-macula	Q5	0.444 (0.351 - 0.562)	1.07E-10	0.658 (0.519 - 0.835)	0.024231
Curve Angle (artery)	Q2	0.830 (0.673 - 1.023)	0.135792	1.000 (0.810 - 1.233)	0.998115
Curve Angle (artery)	Q3	0.726 (0.585 - 0.902)	0.009226	0.958 (0.771 - 1.191)	0.879586
Curve Angle (artery)	Q4	0.627 (0.500 - 0.786)	0.000168	0.845 (0.673 - 1.060)	0.383891
Curve Angle (artery)	Q5	0.660 (0.528 - 0.825)	0.00074	0.907 (0.725 - 1.135)	0.647108
Curve Angle (vein)	Q2	0.912 (0.731 - 1.138)	0.514974	1.040 (0.833 - 1.297)	0.892402
Curve Angle (vein)	Q3	0.800 (0.636 - 1.005)	0.097198	0.933 (0.742 - 1.173)	0.775757
Curve Angle (vein)	Q4	0.881 (0.705 - 1.100)	0.359544	1.022 (0.817 - 1.278)	0.935829
Curve Angle (vein)	Q5	0.925 (0.742 - 1.152)	0.573293	1.013 (0.812 - 1.263)	0.972889
Curve Angle-macula	Q2	0.954 (0.766 - 1.189)	0.748837	1.046 (0.839 - 1.303)	0.875518
Curve Angle-macula	Q3	0.852 (0.680 - 1.069)	0.247442	0.977 (0.778 - 1.225)	0.932258
Curve Angle-macula	Q4	0.848 (0.676 - 1.063)	0.233015	0.962 (0.767 - 1.207)	0.893228
Curve Angle-macula	Q5	0.926 (0.742 - 1.156)	0.58423	0.990 (0.793 - 1.236)	0.983246
Chord length (artery)	Q2	1.368 (1.025 - 1.827)	0.064649	1.001 (0.748 - 1.339)	0.998115
Chord length (artery)	Q3	1.698 (1.286 - 2.241)	0.000556	0.967 (0.729 - 1.284)	0.93115
Chord length (artery)	Q4	2.314 (1.777 - 3.015)	3.02E-09	1.090 (0.829 - 1.434)	0.763176
Chord length (artery)	Q5	3.421 (2.660 - 4.399)	3.34E-20	1.322 (1.012 - 1.726)	0.216405
Chord length (vein)	Q2	1.117 (0.859 - 1.453)	0.505859	0.947 (0.727 - 1.234)	0.875177
Chord length (vein)	Q3	1.400 (1.089 - 1.799)	0.019245	1.029 (0.799 - 1.326)	0.93149
Chord length (vein)	Q4	1.415 (1.101 - 1.819)	0.015356	0.892 (0.691 - 1.153)	0.647027
Chord length (vein)	Q5	2.411 (1.917 - 3.031)	6.32E-13	1.224 (0.964 - 1.553)	0.316535
Chord length-macula	Q2	1.222 (0.937 - 1.595)	0.215031	1.078 (0.826 - 1.407)	0.799178
Chord length-macula	Q3	1.553 (1.206 - 2.000)	0.001746	1.254 (0.972 - 1.617)	0.294139
Chord length-macula	Q4	1.622 (1.261 - 2.086)	0.000489	1.211 (0.940 - 1.560)	0.375737

Chord length-macula	Q5	2.327 (1.836 - 2.949)	2.43E-11	1.421 (1.117 - 1.809)	0.071337
Central Retinal Artery Equivalent	Q2	0.813 (0.660 - 1.001)	0.092174	0.893 (0.725 - 1.101)	0.560679
Central Retinal Artery Equivalent	Q3	0.812 (0.659 - 1.000)	0.089512	0.981 (0.796 - 1.210)	0.940649
Central Retinal Artery Equivalent	Q4	0.585 (0.466 - 0.735)	1.61E-05	0.775 (0.615 - 0.976)	0.179112
Central Retinal Artery Equivalent	Q5	0.550 (0.436 - 0.694)	1.97E-06	0.830 (0.655 - 1.052)	0.356868
Central Retinal Vein Equivalent	Q2	1.030 (0.825 - 1.286)	0.836342	1.092 (0.874 - 1.364)	0.683994
Central Retinal Vein Equivalent	Q3	0.915 (0.729 - 1.150)	0.54693	0.967 (0.769 - 1.216)	0.911432
Central Retinal Vein Equivalent	Q4	0.901 (0.716 - 1.133)	0.469044	0.971 (0.771 - 1.223)	0.924628
Central Retinal Vein Equivalent	Q5	0.994 (0.795 - 1.242)	0.967565	1.032 (0.823 - 1.293)	0.916292
Squared curvature tortuosity (artery)	Q2	0.886 (0.709 - 1.107)	0.382918	0.907 (0.726 - 1.134)	0.647108
Squared curvature tortuosity (artery)	Q3	0.872 (0.697 - 1.091)	0.316679	0.892 (0.713 - 1.116)	0.5842
Squared curvature tortuosity (artery)	Q4	0.889 (0.712 - 1.111)	0.397309	0.910 (0.728 - 1.137)	0.659882
Squared curvature tortuosity (artery)	Q5	0.893 (0.714 - 1.115)	0.417588	0.835 (0.668 - 1.044)	0.345978
Squared curvature tortuosity (vein)	Q2	1.085 (0.856 - 1.374)	0.58679	1.082 (0.854 - 1.371)	0.745063
Squared curvature tortuosity (vein)	Q3	0.984 (0.772 - 1.253)	0.922378	0.962 (0.755 - 1.226)	0.900468
Squared curvature tortuosity (vein)	Q4	1.295 (1.032 - 1.625)	0.051295	1.248 (0.994 - 1.566)	0.249966
Squared curvature tortuosity (vein)	Q5	1.322 (1.054 - 1.659)	0.031895	1.183 (0.943 - 1.484)	0.383891
Squared curvature tortuosity-macula	Q2	1.058 (0.843 - 1.327)	0.704145	1.109 (0.884 - 1.392)	0.633457
Squared curvature tortuosity-macula	Q3	0.959 (0.760 - 1.209)	0.780889	0.993 (0.787 - 1.252)	0.993367
Squared curvature tortuosity-macula	Q4	0.928 (0.734 - 1.173)	0.614407	0.958 (0.758 - 1.211)	0.888081
Squared curvature tortuosity-macula	Q5	1.209 (0.970 - 1.506)	0.151247	1.177 (0.944 - 1.467)	0.383891
Dractal Dimension (artery)	Q2	0.666 (0.550 - 0.806)	9.86E-05	0.805 (0.664 - 0.976)	0.168444
Dractal Dimension (artery)	Q3	0.481 (0.390 - 0.594)	7.12E-11	0.693 (0.560 - 0.858)	0.027311
Dractal Dimension (artery)	Q4	0.412 (0.330 - 0.513)	4.5E-14	0.742 (0.591 - 0.932)	0.091196
Dractal Dimension (artery)	Q5	0.236 (0.181 - 0.309)	2.24E-23	0.634 (0.476 - 0.845)	0.052553
Fractal Dimension (vessel)	Q2	0.646 (0.532 - 0.785)	3.88E-05	0.757 (0.623 - 0.920)	0.071939
Fractal Dimension (vessel)	Q3	0.465 (0.375 - 0.576)	2.21E-11	0.655 (0.527 - 0.814)	0.010942
Fractal Dimension (vessel)	Q4	0.442 (0.356 - 0.549)	1.87E-12	0.767 (0.613 - 0.959)	0.151763
Fractal Dimension (vessel)	Q5	0.291 (0.226 - 0.373)	1.56E-20	0.753 (0.575 - 0.985)	0.212663
Fractal tortuosity (artery)	Q2	1.234 (0.966 - 1.577)	0.152938	1.108 (0.867 - 1.417)	0.664126

Fractal tortuosity (artery)	Q3	1.038 (0.804 - 1.341)	0.821414	0.847 (0.655 - 1.094)	0.465351
Fractal tortuosity (artery)	Q4	1.342 (1.054 - 1.708)	0.034397	1.013 (0.795 - 1.291)	0.979549
Fractal tortuosity (artery)	Q5	1.965 (1.569 - 2.460)	2.15E-08	1.229 (0.978 - 1.545)	0.290385
Fractal tortuosity (vein)	Q2	1.363 (1.071 - 1.735)	0.02475	1.262 (0.991 - 1.607)	0.249966
Fractal tortuosity (vein)	Q3	1.200 (0.936 - 1.538)	0.230413	1.058 (0.825 - 1.357)	0.84787
Fractal tortuosity (vein)	Q4	1.408 (1.108 - 1.790)	0.012222	1.162 (0.913 - 1.479)	0.492538
Fractal tortuosity (vein)	Q5	1.661 (1.316 - 2.097)	6.71E-05	1.155 (0.913 - 1.461)	0.501993
Fractal tortuosity-macula	Q2	0.976 (0.760 - 1.254)	0.88293	0.923 (0.718 - 1.186)	0.759236
Fractal tortuosity-macula	Q3	1.310 (1.037 - 1.655)	0.047378	1.222 (0.967 - 1.544)	0.30748
Fractal tortuosity-macula	Q4	1.294 (1.023 - 1.637)	0.060991	1.163 (0.919 - 1.471)	0.472167
Fractal tortuosity-macula	Q5	1.497 (1.192 - 1.881)	0.001454	1.201 (0.955 - 1.510)	0.347994
Fractal Dimension (vein)	Q2	0.804 (0.658 - 0.981)	0.061568	0.918 (0.752 - 1.122)	0.658512
Fractal Dimension (vein)	Q3	0.626 (0.506 - 0.775)	5.9E-05	0.815 (0.657 - 1.010)	0.252848
Fractal Dimension (vein)	Q4	0.494 (0.393 - 0.621)	8.93E-09	0.754 (0.598 - 0.952)	0.137843
Fractal Dimension (vein)	Q5	0.469 (0.372 - 0.591)	1.02E-09	0.865 (0.680 - 1.101)	0.504858
Inflection count tortuosity (artery)	Q2	0.829 (0.672 - 1.022)	0.133908	0.948 (0.768 - 1.169)	0.825039
Inflection count tortuosity (artery)	Q3	0.743 (0.599 - 0.921)	0.015713	0.884 (0.712 - 1.097)	0.531479
Inflection count tortuosity (artery)	Q4	0.677 (0.543 - 0.845)	0.00151	0.832 (0.666 - 1.038)	0.330364
Inflection count tortuosity (artery)	Q5	0.604 (0.480 - 0.759)	5.68E-05	0.719 (0.572 - 0.905)	0.071939
Inflection count tortuosity (vein)	Q2	0.806 (0.636 - 1.021)	0.126526	0.853 (0.673 - 1.081)	0.440716
Inflection count tortuosity (vein)	Q3	1.035 (0.829 - 1.292)	0.813984	1.113 (0.891 - 1.390)	0.607434
Inflection count tortuosity (vein)	Q4	0.941 (0.750 - 1.181)	0.682401	1.019 (0.812 - 1.280)	0.945733
Inflection count tortuosity (vein)	Q5	1.090 (0.875 - 1.357)	0.540512	1.161 (0.932 - 1.446)	0.434323
Inflection count tortuosity-macula	Q2	0.789 (0.631 - 0.985)	0.068957	0.869 (0.696 - 1.086)	0.485813
Inflection count tortuosity-macula	Q3	0.832 (0.668 - 1.035)	0.159793	0.952 (0.764 - 1.185)	0.84787
Inflection count tortuosity-macula	Q4	0.738 (0.588 - 0.925)	0.018966	0.819 (0.653 - 1.028)	0.294988
Inflection count tortuosity-macula	Q5	0.875 (0.705 - 1.086)	0.313389	0.952 (0.767 - 1.182)	0.84787
Junctional Exponent Deviation (artery)	Q2	0.942 (0.756 - 1.174)	0.674951	0.997 (0.800 - 1.243)	0.998115
Junctional Exponent Deviation (artery)	Q3	0.789 (0.626 - 0.994)	0.081888	0.834 (0.662 - 1.052)	0.358974
Junctional Exponent Deviation (artery)	Q4	0.779 (0.618 - 0.982)	0.066331	0.828 (0.657 - 1.044)	0.344139

Junctional Exponent Deviation (artery)	Q5	1.079 (0.872 - 1.336)	0.573293	1.023 (0.826 - 1.267)	0.932258
Junctional Exponent Deviation (vein)	Q2	1.012 (0.796 - 1.288)	0.939452	1.035 (0.814 - 1.317)	0.911634
Junctional Exponent Deviation (vein)	Q3	1.051 (0.828 - 1.334)	0.749109	1.060 (0.835 - 1.345)	0.830097
Junctional Exponent Deviation (vein)	Q4	1.267 (1.008 - 1.592)	0.078728	1.218 (0.969 - 1.532)	0.30489
Junctional Exponent Deviation (vein)	Q5	1.371 (1.095 - 1.718)	0.0139	1.155 (0.921 - 1.448)	0.474489
Junctional Exponent Deviation-macula	Q2	0.739 (0.589 - 0.928)	0.020153	0.790 (0.629 - 0.992)	0.219578
Junctional Exponent Deviation-macula	Q3	0.806 (0.646 - 1.006)	0.098673	0.895 (0.717 - 1.117)	0.590634
Junctional Exponent Deviation-macula	Q4	0.777 (0.621 - 0.972)	0.053581	0.836 (0.668 - 1.046)	0.347994
Junctional Exponent Deviation-macula	Q5	0.953 (0.770 - 1.179)	0.731311	0.945 (0.764 - 1.170)	0.814421
Length Diameter Ratio (artery)	Q2	1.168 (0.880 - 1.552)	0.379024	0.901 (0.678 - 1.197)	0.709547
Length Diameter Ratio (artery)	Q3	1.600 (1.226 - 2.088)	0.001475	1.038 (0.793 - 1.358)	0.916292
Length Diameter Ratio (artery)	Q4	2.057 (1.594 - 2.655)	1.44E-07	1.101 (0.848 - 1.430)	0.709547
Length Diameter Ratio (artery)	Q5	2.904 (2.277 - 3.702)	2.15E-16	1.275 (0.988 - 1.644)	0.252848
Length Diameter Ratio (vein)	Q2	0.947 (0.740 - 1.211)	0.736443	0.924 (0.722 - 1.182)	0.757926
Length Diameter Ratio (vein)	Q3	0.954 (0.746 - 1.221)	0.772328	0.880 (0.688 - 1.127)	0.580853
Length Diameter Ratio (vein)	Q4	1.338 (1.065 - 1.680)	0.025454	1.086 (0.863 - 1.367)	0.710746
Length Diameter Ratio (vein)	Q5	1.623 (1.303 - 2.023)	5.62E-05	1.095 (0.875 - 1.371)	0.681444
Length Diameter Ratio-macula	Q2	0.908 (0.700 - 1.179)	0.563808	0.836 (0.644 - 1.085)	0.426872
Length Diameter Ratio-macula	Q3	1.368 (1.080 - 1.734)	0.020758	1.148 (0.906 - 1.456)	0.522677
Length Diameter Ratio-macula	Q4	1.294 (1.017 - 1.645)	0.068097	1.021 (0.802 - 1.300)	0.944285
Length Diameter Ratio-macula	Q5	1.826 (1.458 - 2.287)	7.08E-07	1.227 (0.977 - 1.540)	0.293142
level (artery)	Q2	0.659 (0.536 - 0.809)	0.000215	0.806 (0.655 - 0.991)	0.216405
level (artery)	Q3	0.583 (0.471 - 0.721)	2.87E-06	0.823 (0.664 - 1.021)	0.290385
level (artery)	Q4	0.507 (0.406 - 0.633)	1.12E-08	0.769 (0.614 - 0.963)	0.159128
level (artery)	Q5	0.494 (0.395 - 0.618)	3.84E-09	0.818 (0.652 - 1.026)	0.294988
level (vein)	Q2	0.794 (0.639 - 0.988)	0.072095	0.891 (0.716 - 1.109)	0.562385
level (vein)	Q3	0.799 (0.643 - 0.992)	0.078728	0.930 (0.748 - 1.157)	0.745907
level (vein)	Q4	0.745 (0.598 - 0.930)	0.020279	0.937 (0.750 - 1.170)	0.783584
level (vein)	Q5	0.722 (0.577 - 0.902)	0.009958	0.958 (0.765 - 1.199)	0.881835
level-macula	Q2	0.910 (0.732 - 1.132)	0.496523	1.010 (0.813 - 1.256)	0.983246

level-macula	Q3	0.828 (0.662 - 1.035)	0.158384	0.947 (0.757 - 1.184)	0.830097
level-macula	Q4	0.860 (0.690 - 1.073)	0.266761	1.016 (0.814 - 1.267)	0.958649
level-macula	Q5	0.780 (0.622 - 0.979)	0.061568	0.925 (0.737 - 1.161)	0.7346
Linear regression tortuosity (artery)	Q2	0.907 (0.728 - 1.130)	0.482498	0.978 (0.785 - 1.218)	0.932262
Linear regression tortuosity (artery)	Q3	0.872 (0.698 - 1.089)	0.313389	0.942 (0.754 - 1.177)	0.808841
Linear regression tortuosity (artery)	Q4	0.809 (0.645 - 1.015)	0.115405	0.880 (0.701 - 1.103)	0.535544
Linear regression tortuosity (artery)	Q5	0.884 (0.708 - 1.102)	0.369791	0.901 (0.722 - 1.125)	0.622254
Linear regression tortuosity (vein)	Q2	1.035 (0.830 - 1.290)	0.813984	1.113 (0.893 - 1.388)	0.604218
Linear regression tortuosity (vein)	Q3	0.921 (0.735 - 1.155)	0.571614	1.001 (0.798 - 1.255)	0.998115
Linear regression tortuosity (vein)	Q4	0.864 (0.686 - 1.088)	0.303427	0.907 (0.720 - 1.142)	0.658512
Linear regression tortuosity (vein)	Q5	0.976 (0.780 - 1.221)	0.86788	1.005 (0.804 - 1.257)	0.996454
Linear regression tortuosity-macula	Q2	1.118 (0.896 - 1.395)	0.423979	1.168 (0.936 - 1.457)	0.416444
Linear regression tortuosity-macula	Q3	0.958 (0.761 - 1.206)	0.775357	1.006 (0.799 - 1.266)	0.996454
Linear regression tortuosity-macula	Q4	0.889 (0.703 - 1.124)	0.423979	0.915 (0.724 - 1.157)	0.698831
Linear regression tortuosity-macula	Q5	1.089 (0.871 - 1.361)	0.552659	1.093 (0.875 - 1.367)	0.681444
Number of bifurcation points (artery)	Q2	0.777 (0.643 - 0.939)	0.019802	0.954 (0.788 - 1.154)	0.82829
Number of bifurcation points (artery)	Q3	0.495 (0.400 - 0.612)	6.07E-10	0.731 (0.590 - 0.907)	0.071939
Number of bifurcation points (artery)	Q4	0.433 (0.345 - 0.544)	6.28E-12	0.785 (0.621 - 0.993)	0.220251
Number of bifurcation points (artery)	Q5	0.306 (0.237 - 0.394)	2.85E-18	0.776 (0.592 - 1.017)	0.261759
Number of bifurcation points (vein)	Q2	0.785 (0.642 - 0.961)	0.038121	0.922 (0.753 - 1.129)	0.681444
Number of bifurcation points (vein)	Q3	0.594 (0.477 - 0.738)	1.08E-05	0.799 (0.642 - 0.996)	0.225362
Number of bifurcation points (vein)	Q4	0.635 (0.513 - 0.786)	0.000104	0.947 (0.762 - 1.178)	0.82829
Number of bifurcation points (vein)	Q5	0.500 (0.395 - 0.633)	4.17E-08	0.912 (0.715 - 1.163)	0.698831
Number of bifurcation points-macula	Q2	0.692 (0.562 - 0.851)	0.001409	0.825 (0.670 - 1.016)	0.274082
Number of bifurcation points-macula	Q3	0.696 (0.571 - 0.850)	0.00107	0.939 (0.768 - 1.148)	0.763564
Number of bifurcation points-macula	Q4	0.528 (0.420 - 0.665)	2.47E-07	0.803 (0.637 - 1.013)	0.25875
Number of bifurcation points-macula	Q5	0.439 (0.347 - 0.556)	6.92E-11	0.804 (0.632 - 1.024)	0.290943
Number of branching points (artery)	Q2	0.647 (0.532 - 0.785)	3.88E-05	0.789 (0.649 - 0.959)	0.137843
Number of branching points (artery)	Q3	0.542 (0.443 - 0.663)	1.52E-08	0.792 (0.645 - 0.972)	0.167598
Number of branching points (artery)	Q4	0.388 (0.310 - 0.485)	1.84E-15	0.723 (0.574 - 0.911)	0.072357

Number of branching points (artery)	Q5	0.243 (0.185 - 0.319)	2.3E-22	0.660 (0.493 - 0.883)	0.071939
Number of branching points (vein)	Q2	0.714 (0.587 - 0.869)	0.002003	0.856 (0.703 - 1.042)	0.356868
Number of branching points (vein)	Q3	0.533 (0.426 - 0.665)	1.38E-07	0.737 (0.589 - 0.922)	0.083163
Number of branching points (vein)	Q4	0.544 (0.440 - 0.674)	1.16E-07	0.900 (0.723 - 1.120)	0.606322
Number of branching points (vein)	Q5	0.380 (0.298 - 0.484)	8.93E-14	0.771 (0.598 - 0.995)	0.225362
Number of branching points-macula	Q2	0.675 (0.554 - 0.823)	0.000318	0.800 (0.655 - 0.976)	0.169149
Number of branching points-macula	Q3	0.482 (0.388 - 0.600)	4.01E-10	0.666 (0.534 - 0.830)	0.017112
Number of branching points-macula	Q4	0.518 (0.415 - 0.646)	2.81E-08	0.817 (0.652 - 1.023)	0.290943
Number of branching points-macula	Q5	0.429 (0.342 - 0.540)	4.06E-12	0.825 (0.652 - 1.044)	0.344139
N_nonterminal (artery)	Q2	0.681 (0.564 - 0.823)	0.000209	0.833 (0.689 - 1.007)	0.249966
N_nonterminal (artery)	Q3	0.477 (0.386 - 0.590)	7.19E-11	0.710 (0.572 - 0.881)	0.052553
N_nonterminal (artery)	Q4	0.401 (0.321 - 0.501)	1.4E-14	0.766 (0.608 - 0.965)	0.164614
N_nonterminal (artery)	Q5	0.250 (0.191 - 0.327)	2.77E-22	0.720 (0.539 - 0.960)	0.167598
N_nonterminal (vein)	Q2	0.613 (0.500 - 0.751)	9.86E-06	0.739 (0.602 - 0.906)	0.064874
N_nonterminal (vein)	Q3	0.597 (0.486 - 0.733)	3.7E-06	0.863 (0.701 - 1.063)	0.412995
N_nonterminal (vein)	Q4	0.516 (0.416 - 0.641)	1.23E-08	0.873 (0.699 - 1.091)	0.503569
N_nonterminal (vein)	Q5	0.377 (0.295 - 0.481)	7.19E-14	0.806 (0.623 - 1.042)	0.322049
Number of vessel segments (artery)	Q2	0.687 (0.569 - 0.829)	0.000276	0.829 (0.686 - 1.002)	0.242962
Number of vessel segments (artery)	Q3	0.442 (0.356 - 0.548)	1.19E-12	0.654 (0.525 - 0.814)	0.010942
Number of vessel segments (artery)	Q4	0.409 (0.329 - 0.509)	1.86E-14	0.773 (0.616 - 0.971)	0.168444
Number of vessel segments (artery)	Q5	0.232 (0.176 - 0.305)	2.24E-23	0.673 (0.501 - 0.903)	0.084095
Number of vessel segments (vein)	Q2	0.618 (0.505 - 0.756)	1.19E-05	0.738 (0.603 - 0.904)	0.062531
Number of vessel segments (vein)	Q3	0.583 (0.473 - 0.719)	1.88E-06	0.831 (0.672 - 1.027)	0.294988
Number of vessel segments (vein)	Q4	0.503 (0.405 - 0.624)	2.57E-09	0.843 (0.676 - 1.051)	0.364374
Number of vessel segments (vein)	Q5	0.356 (0.279 - 0.453)	1.48E-15	0.778 (0.602 - 1.006)	0.249966
Number of vessel segments-macula	Q2	0.612 (0.503 - 0.746)	4.61E-06	0.738 (0.605 - 0.899)	0.056363
Number of vessel segments-macula	Q3	0.463 (0.373 - 0.575)	2.43E-11	0.671 (0.539 - 0.834)	0.017213
Number of vessel segments-macula	Q4	0.417 (0.334 - 0.522)	2.73E-13	0.709 (0.564 - 0.891)	0.062531
Number of vessel segments-macula	Q5	0.405 (0.321 - 0.509)	1.76E-13	0.856 (0.674 - 1.089)	0.465351
N_terminal (artery)	Q2	0.677 (0.561 - 0.817)	0.000159	0.828 (0.685 - 1.001)	0.242545

N_terminal (artery)	Q3	0.462 (0.375 - 0.570)	6.28E-12	0.682 (0.551 - 0.845)	0.0216
N_terminal (artery)	Q4	0.385 (0.308 - 0.481)	1.24E-15	0.732 (0.580 - 0.923)	0.084095
N_terminal (artery)	Q5	0.231 (0.176 - 0.304)	2.35E-23	0.674 (0.501 - 0.906)	0.085128
N_terminal (vein)	Q2	0.662 (0.544 - 0.805)	0.000114	0.792 (0.651 - 0.964)	0.151763
N_terminal (vein)	Q3	0.513 (0.413 - 0.635)	6.17E-09	0.732 (0.589 - 0.910)	0.071939
N_terminal (vein)	Q4	0.492 (0.394 - 0.613)	1.79E-09	0.837 (0.668 - 1.050)	0.356868
N_terminal (vein)	Q5	0.382 (0.300 - 0.486)	7.9E-14	0.858 (0.664 - 1.108)	0.504858
Number of vessel tree (artery)	Q2	0.920 (0.763 - 1.109)	0.479511	0.996 (0.826 - 1.201)	0.996454
Number of vessel tree (artery)	Q3	0.848 (0.663 - 1.084)	0.272683	0.983 (0.769 - 1.257)	0.958649
Number of vessel tree (artery)	Q4	0.687 (0.545 - 0.867)	0.003975	0.826 (0.655 - 1.043)	0.341362
Number of vessel tree (artery)	Q5	0.744 (0.595 - 0.931)	0.021165	0.932 (0.745 - 1.167)	0.763564
Number of vessel tree (vein)	Q2	0.967 (0.771 - 1.212)	0.821414	1.040 (0.830 - 1.304)	0.892402
Number of vessel tree (vein)	Q3	0.956 (0.792 - 1.153)	0.714577	1.043 (0.864 - 1.258)	0.85133
Number of vessel tree (vein)	Q4	0.829 (0.666 - 1.033)	0.154172	0.924 (0.742 - 1.151)	0.710746
Number of vessel tree (vein)	Q5	0.723 (0.562 - 0.929)	0.023897	0.826 (0.642 - 1.062)	0.372942
Number of vessel tree-macula	Q2	0.998 (0.798 - 1.247)	0.987132	1.038 (0.831 - 1.298)	0.893228
Number of vessel tree-macula	Q3	1.032 (0.825 - 1.291)	0.829477	1.103 (0.881 - 1.380)	0.647108
Number of vessel tree-macula	Q4	1.007 (0.826 - 1.226)	0.962892	1.070 (0.878 - 1.304)	0.734652
Number of vessel tree-macula	Q5	0.815 (0.653 - 1.018)	0.123498	0.900 (0.720 - 1.124)	0.616357
Strahler (artery)	Q2	0.682 (0.556 - 0.837)	0.000711	0.853 (0.695 - 1.047)	0.364374
Strahler (artery)	Q3	0.602 (0.487 - 0.743)	9.74E-06	0.837 (0.677 - 1.036)	0.326145
Strahler (artery)	Q4	0.487 (0.388 - 0.610)	2.73E-09	0.726 (0.578 - 0.912)	0.072357
Strahler (artery)	Q5	0.497 (0.397 - 0.622)	6.01E-09	0.793 (0.632 - 0.996)	0.225362
Strahler (vein)	Q2	0.861 (0.687 - 1.080)	0.28092	0.966 (0.771 - 1.212)	0.908759
Strahler (vein)	Q3	0.876 (0.699 - 1.097)	0.341072	1.042 (0.831 - 1.306)	0.888387
Strahler (vein)	Q4	1.002 (0.807 - 1.246)	0.987132	1.212 (0.974 - 1.508)	0.294988
Strahler (vein)	Q5	0.854 (0.681 - 1.071)	0.254904	1.004 (0.799 - 1.260)	0.998115
Strahler-macula	Q2	0.892 (0.719 - 1.106)	0.39592	1.031 (0.831 - 1.279)	0.916011
Strahler-macula	Q3	0.732 (0.583 - 0.918)	0.01604	0.886 (0.706 - 1.112)	0.561287
Strahler-macula	Q4	0.733 (0.585 - 0.920)	0.016418	0.900 (0.717 - 1.129)	0.62757

Strahler-macula	Q5	0.874 (0.704 - 1.084)	0.30971	1.082 (0.871 - 1.344)	0.710746
Tortuosity Density (artery)	Q2	1.024 (0.822 - 1.275)	0.868412	1.102 (0.884 - 1.372)	0.647027
Tortuosity Density (artery)	Q3	1.027 (0.825 - 1.279)	0.85229	1.103 (0.885 - 1.373)	0.647027
Tortuosity Density (artery)	Q4	0.846 (0.672 - 1.065)	0.234881	0.905 (0.718 - 1.139)	0.647108
Tortuosity Density (artery)	Q5	0.847 (0.672 - 1.067)	0.240596	0.814 (0.646 - 1.026)	0.294139
Tortuosity Density (vein)	Q2	1.130 (0.887 - 1.439)	0.422667	1.104 (0.867 - 1.406)	0.673689
Tortuosity Density (vein)	Q3	1.263 (0.997 - 1.598)	0.093552	1.209 (0.955 - 1.531)	0.347994
Tortuosity Density (vein)	Q4	1.284 (1.015 - 1.624)	0.070473	1.179 (0.932 - 1.492)	0.416444
Tortuosity Density (vein)	Q5	1.396 (1.108 - 1.759)	0.011233	1.187 (0.941 - 1.496)	0.383891
Tortuosity Density-macula	Q2	0.832 (0.664 - 1.042)	0.174273	0.886 (0.707 - 1.109)	0.560679
Tortuosity Density-macula	Q3	0.785 (0.624 - 0.986)	0.070899	0.843 (0.671 - 1.060)	0.382079
Tortuosity Density-macula	Q4	0.858 (0.687 - 1.073)	0.265433	0.886 (0.709 - 1.108)	0.560679
Tortuosity Density-macula	Q5	1.003 (0.809 - 1.243)	0.987132	0.976 (0.787 - 1.211)	0.931803
Distance-based tortuosity (artery)	Q2	1.152 (0.922 - 1.438)	0.302957	1.300 (1.040 - 1.623)	0.154948
Distance-based tortuosity (artery)	Q3	0.999 (0.794 - 1.257)	0.992851	1.132 (0.900 - 1.425)	0.560679
Distance-based tortuosity (artery)	Q4	0.942 (0.746 - 1.189)	0.696232	1.072 (0.849 - 1.354)	0.780866
Distance-based tortuosity (artery)	Q5	1.041 (0.829 - 1.307)	0.786775	1.150 (0.915 - 1.444)	0.501993
Distance-based tortuosity (vein)	Q2	1.120 (0.889 - 1.412)	0.436092	1.185 (0.940 - 1.494)	0.387326
Distance-based tortuosity (vein)	Q3	1.098 (0.870 - 1.385)	0.530693	1.150 (0.912 - 1.452)	0.504858
Distance-based tortuosity (vein)	Q4	1.189 (0.947 - 1.494)	0.211442	1.191 (0.947 - 1.496)	0.371107
Distance-based tortuosity (vein)	Q5	1.112 (0.882 - 1.401)	0.469044	1.087 (0.862 - 1.371)	0.710746
Distance-based tortuosity-macula	Q2	1.179 (0.937 - 1.483)	0.240596	1.240 (0.985 - 1.560)	0.262348
Distance-based tortuosity-macula	Q3	1.137 (0.903 - 1.433)	0.371375	1.202 (0.954 - 1.515)	0.350911
Distance-based tortuosity-macula	Q4	1.060 (0.838 - 1.341)	0.705887	1.079 (0.853 - 1.366)	0.754709
Distance-based tortuosity-macula	Q5	1.167 (0.927 - 1.468)	0.273829	1.148 (0.912 - 1.445)	0.504858
Twist-based tortuosity (artery)	Q2	1.033 (0.875 - 1.219)	0.766377	1.096 (0.929 - 1.294)	0.552297
Twist-based tortuosity (artery)	Q3	0.877 (0.700 - 1.097)	0.341834	0.917 (0.733 - 1.148)	0.695577
Twist-based tortuosity (artery)	Q4	1.013 (0.793 - 1.295)	0.936536	1.007 (0.788 - 1.287)	0.993367
Twist-based tortuosity (vein)	Q2	1.038 (0.866 - 1.246)	0.751179	1.003 (0.836 - 1.203)	0.998115
Twist-based tortuosity (vein)	Q3	1.287 (1.051 - 1.577)	0.030184	1.178 (0.961 - 1.443)	0.347994

Twist-based tortuosity (vein)	Q4	1.210 (0.926 - 1.581)	0.24401	1.044 (0.798 - 1.365)	0.900468
Twist-based tortuosity-macula	Q2	1.000 (0.816 - 1.225)	0.999466	0.996 (0.813 - 1.221)	0.998115
Twist-based tortuosity-macula	Q3	1.293 (1.055 - 1.586)	0.027526	1.295 (1.056 - 1.588)	0.107443
Twist-based tortuosity-macula	Q4	1.076 (0.836 - 1.385)	0.654622	1.041 (0.809 - 1.341)	0.900468
Twist-based tortuosity-macula	Q5	1.188 (0.958 - 1.474)	0.183112	1.114 (0.898 - 1.381)	0.590634
Vessel Area Density	Q2	0.699 (0.574 - 0.851)	0.001046	0.809 (0.664 - 0.986)	0.199589
Vessel Area Density	Q3	0.573 (0.465 - 0.705)	7.03E-07	0.762 (0.617 - 0.939)	0.093999
Vessel Area Density	Q4	0.444 (0.355 - 0.556)	1.35E-11	0.722 (0.574 - 0.908)	0.072249
Vessel Area Density	Q5	0.338 (0.264 - 0.432)	1.33E-16	0.742 (0.573 - 0.961)	0.164614
Vessel Area Density (artery)	Q2	0.715 (0.592 - 0.864)	0.001409	0.847 (0.700 - 1.024)	0.294988
Vessel Area Density (artery)	Q3	0.447 (0.360 - 0.556)	4.47E-12	0.637 (0.511 - 0.795)	0.007408
Vessel Area Density (artery)	Q4	0.426 (0.341 - 0.530)	3.72E-13	0.743 (0.592 - 0.932)	0.091196
Vessel Area Density (artery)	Q5	0.268 (0.207 - 0.347)	1.05E-21	0.680 (0.516 - 0.896)	0.072357
Vessel Area Density (artery)-macula	Q2	0.621 (0.510 - 0.756)	8.09E-06	0.754 (0.619 - 0.919)	0.071939
Vessel Area Density (artery)-macula	Q3	0.534 (0.435 - 0.655)	1.12E-08	0.791 (0.642 - 0.974)	0.168444
Vessel Area Density (artery)-macula	Q4	0.385 (0.306 - 0.483)	4.29E-15	0.670 (0.531 - 0.847)	0.027311
Vessel Area Density (artery)-macula	Q5	0.309 (0.242 - 0.395)	2.44E-19	0.697 (0.540 - 0.901)	0.072357
Vessel Area Density (artery)-other	Q2	0.744 (0.613 - 0.902)	0.006657	0.875 (0.721 - 1.063)	0.428429
Vessel Area Density (artery)-other	Q3	0.574 (0.466 - 0.707)	7.59E-07	0.797 (0.645 - 0.983)	0.192991
Vessel Area Density (artery)-other	Q4	0.429 (0.341 - 0.538)	3.12E-12	0.723 (0.573 - 0.913)	0.072938
Vessel Area Density (artery)-other	Q5	0.312 (0.242 - 0.401)	5.44E-18	0.737 (0.564 - 0.964)	0.167598
Vessel Area Density (vein)	Q2	0.760 (0.618 - 0.936)	0.02118	0.882 (0.716 - 1.086)	0.504858
Vessel Area Density (vein)	Q3	0.727 (0.589 - 0.896)	0.007084	0.907 (0.735 - 1.121)	0.629881
Vessel Area Density (vein)	Q4	0.594 (0.476 - 0.741)	1.57E-05	0.850 (0.679 - 1.064)	0.395407
Vessel Area Density (vein)	Q5	0.493 (0.390 - 0.623)	1.66E-08	0.792 (0.623 - 1.008)	0.249966
Vessel Area Density (vein)-macula	Q2	0.787 (0.641 - 0.967)	0.045351	0.902 (0.734 - 1.108)	0.590634
Vessel Area Density (vein)-macula	Q3	0.618 (0.496 - 0.769)	5.9E-05	0.807 (0.647 - 1.007)	0.249966
Vessel Area Density (vein)-macula	Q4	0.610 (0.490 - 0.760)	3.72E-05	0.903 (0.722 - 1.128)	0.629881
Vessel Area Density (vein)-macula	Q5	0.549 (0.438 - 0.689)	9.36E-07	0.892 (0.708 - 1.124)	0.598153
Vessel Area Density (vein)-other	Q2	0.905 (0.739 - 1.110)	0.436402	1.018 (0.831 - 1.248)	0.940649

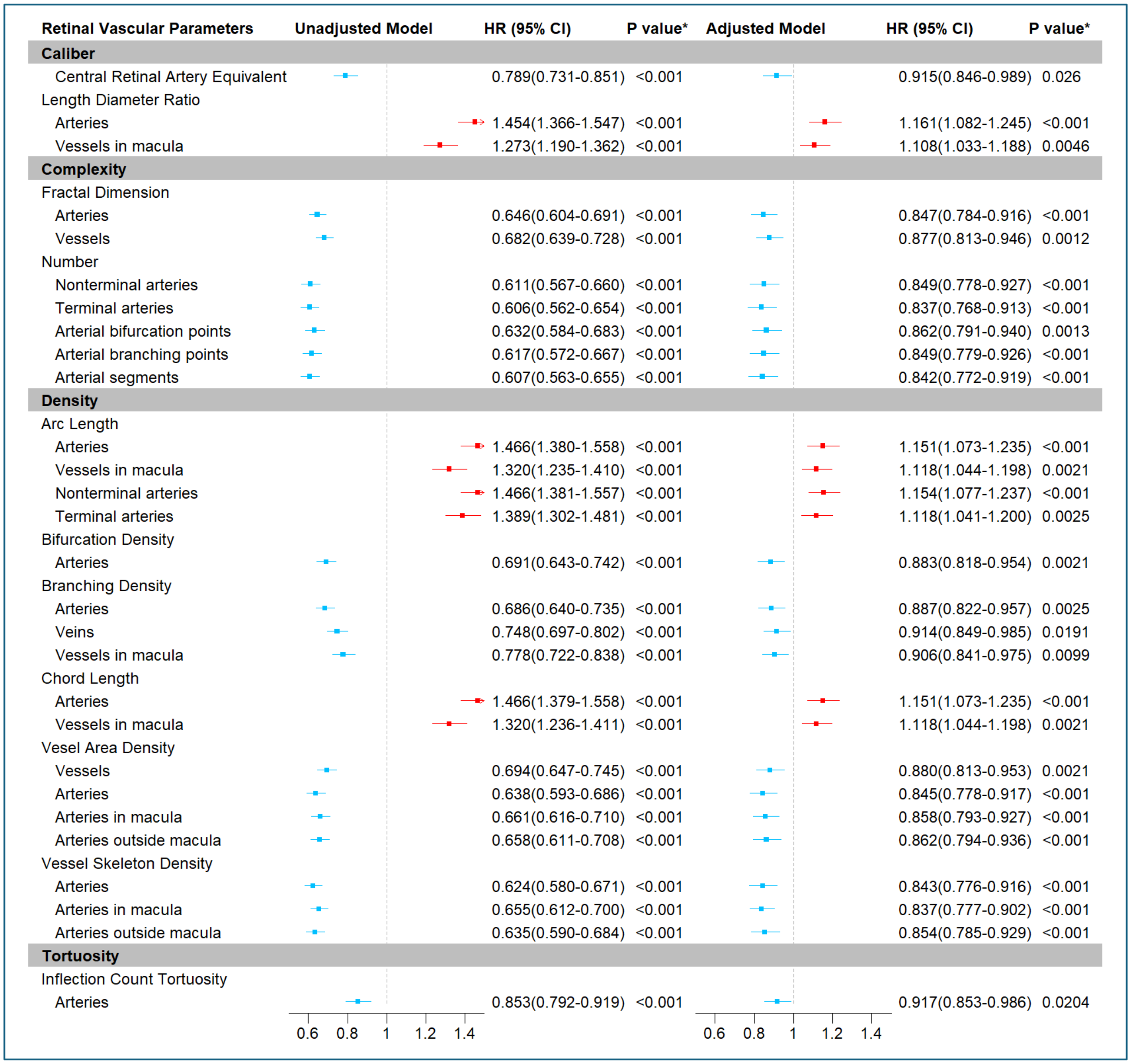
Vessel Area Density (vein)-other	Q3	0.668 (0.535 - 0.832)	0.000961	0.800 (0.641 - 0.999)	0.234318
Vessel Area Density (vein)-other	Q4	0.661 (0.530 - 0.824)	0.00069	0.877 (0.702 - 1.097)	0.518259
Vessel Area Density (vein)-other	Q5	0.543 (0.430 - 0.685)	1.25E-06	0.778 (0.613 - 0.988)	0.212663
Vessel Skeleton Density (artery)	Q2	0.666 (0.550 - 0.806)	9.86E-05	0.809 (0.668 - 0.980)	0.181132
Vessel Skeleton Density (artery)	Q3	0.498 (0.404 - 0.613)	3.77E-10	0.719 (0.582 - 0.888)	0.054536
Vessel Skeleton Density (artery)	Q4	0.391 (0.312 - 0.489)	4.41E-15	0.723 (0.573 - 0.912)	0.072357
Vessel Skeleton Density (artery)	Q5	0.248 (0.190 - 0.323)	5.01E-23	0.684 (0.515 - 0.908)	0.084311
Vessel Skeleton Density (artery)-macula	Q2	0.657 (0.542 - 0.796)	6E-05	0.773 (0.638 - 0.938)	0.085128
Vessel Skeleton Density (artery)-macula	Q3	0.487 (0.395 - 0.601)	1.34E-10	0.717 (0.580 - 0.887)	0.054536
Vessel Skeleton Density (artery)-macula	Q4	0.378 (0.301 - 0.475)	1.38E-15	0.671 (0.532 - 0.848)	0.027311
Vessel Skeleton Density (artery)-macula	Q5	0.283 (0.220 - 0.364)	4.03E-21	0.640 (0.492 - 0.832)	0.027311
Vessel Skeleton Density (artery)-other	Q2	0.683 (0.565 - 0.826)	0.000259	0.809 (0.668 - 0.979)	0.176985
Vessel Skeleton Density (artery)-other	Q3	0.444 (0.357 - 0.552)	2.59E-12	0.631 (0.507 - 0.787)	0.00652
Vessel Skeleton Density (artery)-other	Q4	0.443 (0.357 - 0.549)	1.67E-12	0.793 (0.634 - 0.992)	0.217174
Vessel Skeleton Density (artery)-other	Q5	0.250 (0.192 - 0.325)	7E-23	0.649 (0.490 - 0.860)	0.056363
Vessel Skeleton Density (vein)	Q2	0.767 (0.630 - 0.934)	0.018425	0.870 (0.715 - 1.060)	0.412995
Vessel Skeleton Density (vein)	Q3	0.543 (0.437 - 0.675)	1.65E-07	0.722 (0.580 - 0.898)	0.062531
Vessel Skeleton Density (vein)	Q4	0.492 (0.394 - 0.614)	2.57E-09	0.804 (0.640 - 1.009)	0.250511
Vessel Skeleton Density (vein)	Q5	0.405 (0.320 - 0.513)	8.26E-13	0.846 (0.660 - 1.085)	0.440716
Vessel Skeleton Density (vein)-macula	Q2	0.747 (0.609 - 0.916)	0.012222	0.847 (0.691 - 1.039)	0.344564
Vessel Skeleton Density (vein)-macula	Q3	0.611 (0.492 - 0.758)	2.76E-05	0.838 (0.674 - 1.041)	0.344139
Vessel Skeleton Density (vein)-macula	Q4	0.495 (0.393 - 0.623)	1.07E-08	0.776 (0.615 - 0.980)	0.190772
Vessel Skeleton Density (vein)-macula	Q5	0.560 (0.450 - 0.698)	1.04E-06	1.018 (0.811 - 1.279)	0.950307
Vessel Skeleton Density (vein)-other	Q2	0.822 (0.677 - 0.998)	0.086525	0.949 (0.781 - 1.153)	0.808408
Vessel Skeleton Density (vein)-other	Q3	0.491 (0.392 - 0.616)	4.58E-09	0.652 (0.519 - 0.818)	0.015622
Vessel Skeleton Density (vein)-other	Q4	0.532 (0.427 - 0.662)	8.9E-08	0.841 (0.672 - 1.052)	0.364374
Vessel Skeleton Density (vein)-other	Q5	0.426 (0.337 - 0.539)	9.72E-12	0.866 (0.677 - 1.107)	0.518259
Width (artery)	Q2	0.924 (0.739 - 1.157)	0.579749	0.961 (0.768 - 1.204)	0.892402
Width (artery)	Q3	0.829 (0.658 - 1.045)	0.179016	0.871 (0.690 - 1.099)	0.509092
Width (artery)	Q4	0.900 (0.718 - 1.128)	0.462131	0.919 (0.731 - 1.156)	0.709547

Width (artery)	Q5	1.065 (0.857 - 1.322)	0.65518	0.999 (0.799 - 1.249)	0.998115
Width (vein)	Q2	1.256 (0.962 - 1.640)	0.153763	1.164 (0.891 - 1.520)	0.533418
Width (vein)	Q3	1.567 (1.214 - 2.023)	0.001514	1.286 (0.995 - 1.661)	0.249966
Width (vein)	Q4	1.639 (1.273 - 2.111)	0.000392	1.184 (0.917 - 1.529)	0.449035
Width (vein)	Q5	2.367 (1.865 - 3.005)	1.34E-11	1.402 (1.099 - 1.789)	0.072938
Width (macula)	Q2	0.868 (0.694 - 1.086)	0.303427	0.911 (0.729 - 1.140)	0.669767
Width (macula)	Q3	0.799 (0.636 - 1.004)	0.096137	0.842 (0.670 - 1.059)	0.382079
Width (macula)	Q4	0.806 (0.641 - 1.012)	0.110252	0.842 (0.670 - 1.059)	0.380702
Width (macula)	Q5	1.060 (0.856 - 1.312)	0.674951	0.968 (0.781 - 1.200)	0.908759
Width (nonterminal artery)	Q2	0.799 (0.639 - 1.000)	0.090036	0.850 (0.679 - 1.064)	0.395407
Width (nonterminal artery)	Q3	0.801 (0.641 - 1.002)	0.093034	0.886 (0.707 - 1.109)	0.560679
Width (nonterminal artery)	Q4	0.833 (0.668 - 1.040)	0.171183	0.911 (0.728 - 1.139)	0.665746
Width (nonterminal artery)	Q5	0.905 (0.728 - 1.124)	0.464567	0.949 (0.760 - 1.186)	0.842751
Width (nonterminal vein)	Q2	1.185 (0.916 - 1.532)	0.28092	1.108 (0.857 - 1.433)	0.681444
Width (nonterminal vein)	Q3	1.291 (1.003 - 1.662)	0.08636	1.098 (0.852 - 1.414)	0.709547
Width (nonterminal vein)	Q4	1.530 (1.199 - 1.953)	0.001716	1.183 (0.925 - 1.513)	0.43014
Width (nonterminal vein)	Q5	2.058 (1.632 - 2.595)	6.17E-09	1.308 (1.033 - 1.656)	0.167598
Width (terminal artery)	Q2	1.135 (0.896 - 1.437)	0.393052	1.040 (0.820 - 1.318)	0.900076
Width (terminal artery)	Q3	0.910 (0.709 - 1.169)	0.556415	0.783 (0.609 - 1.007)	0.249966
Width (terminal artery)	Q4	1.172 (0.926 - 1.482)	0.272683	0.863 (0.680 - 1.096)	0.501221
Width (terminal artery)	Q5	1.667 (1.339 - 2.076)	1.87E-05	1.028 (0.820 - 1.290)	0.925639
Width (terminal vein)	Q2	1.179 (0.904 - 1.537)	0.313389	1.010 (0.774 - 1.318)	0.988723
Width (terminal vein)	Q3	1.391 (1.076 - 1.798)	0.02475	1.040 (0.803 - 1.347)	0.908759
Width (terminal vein)	Q4	1.887 (1.480 - 2.404)	1.26E-06	1.204 (0.941 - 1.540)	0.380137
Width (terminal vein)	Q5	2.150 (1.695 - 2.728)	1.95E-09	1.139 (0.892 - 1.455)	0.561287

The Adjusted Model was adjusted for age, sex, systolic blood pressure, total cholesterol, HDL, HbA1c, smoking, BMI, and Indices of Multiple Deprivation at baseline. * The False Discovery Rate method was used to adjust P values in both models at a level of 0.05. HDL indicates high-density lipoprotein; HbA1c, glycosylated hemoglobin; BMI, body mass index; HR, hazard ratio, and CI, Confidence Interval.

Supplementary Figure 3. Sensitivity Analysis for Associations between retinal vascular parameters and risk of incident stroke

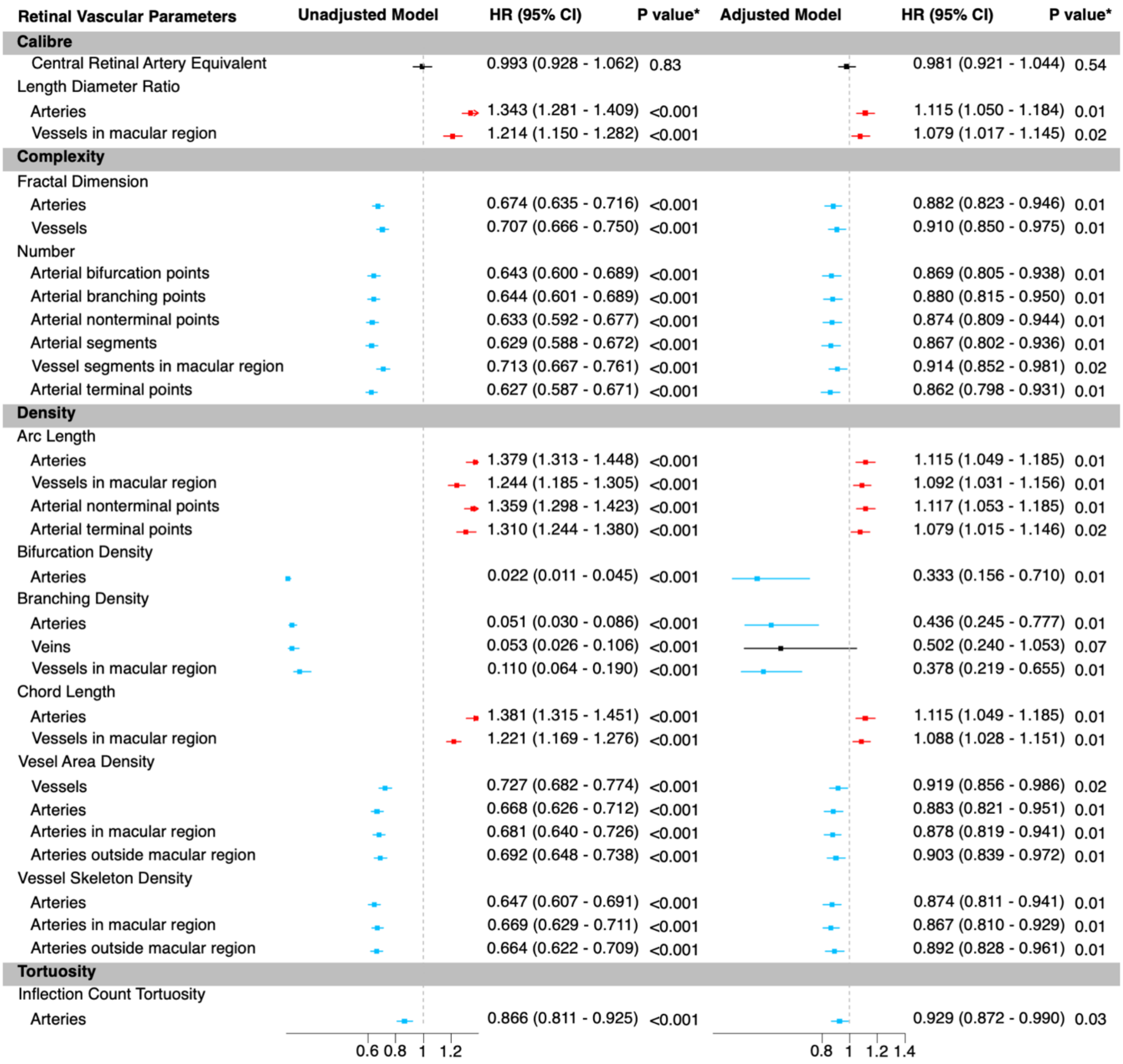
A. sensitivity analyses wherein individuals with a follow-up time of less than three years were excluded (N=44963)



Retinal Vascular Parameters	Unadjusted Model	HR (95% CI)	P value*	Adjusted Model	HR (95% CI)	P value*
Caliber						
Central Retinal Artery Equivalent		0.789(0.731-0.851)	<0.001		0.915(0.846-0.989)	0.026
Length Diameter Ratio						
Arteries		1.454(1.366-1.547)	<0.001		1.161(1.082-1.245)	<0.001
Vessels in macula		1.273(1.190-1.362)	<0.001		1.108(1.033-1.188)	0.0046
Complexity						
Fractal Dimension						
Arteries		0.646(0.604-0.691)	<0.001		0.847(0.784-0.916)	<0.001
Vessels		0.682(0.639-0.728)	<0.001		0.877(0.813-0.946)	0.0012
Number						
Nonterminal arteries		0.611(0.567-0.660)	<0.001		0.849(0.778-0.927)	<0.001
Terminal arteries		0.606(0.562-0.654)	<0.001		0.837(0.768-0.913)	<0.001
Arterial bifurcation points		0.632(0.584-0.683)	<0.001		0.862(0.791-0.940)	0.0013
Arterial branching points		0.617(0.572-0.667)	<0.001		0.849(0.779-0.926)	<0.001
Arterial segments		0.607(0.563-0.655)	<0.001		0.842(0.772-0.919)	<0.001
Density						
Arc Length						
Arteries		1.466(1.380-1.558)	<0.001		1.151(1.073-1.235)	<0.001
Vessels in macula		1.320(1.235-1.410)	<0.001		1.118(1.044-1.198)	0.0021
Nonterminal arteries		1.466(1.381-1.557)	<0.001		1.154(1.077-1.237)	<0.001
Terminal arteries		1.389(1.302-1.481)	<0.001		1.118(1.041-1.200)	0.0025
Bifurcation Density						
Arteries		0.691(0.643-0.742)	<0.001		0.883(0.818-0.954)	0.0021
Branching Density						
Arteries		0.686(0.640-0.735)	<0.001		0.887(0.822-0.957)	0.0025
Veins		0.748(0.697-0.802)	<0.001		0.914(0.849-0.985)	0.0191
Vessels in macula		0.778(0.722-0.838)	<0.001		0.906(0.841-0.975)	0.0099
Chord Length						
Arteries		1.466(1.379-1.558)	<0.001		1.151(1.073-1.235)	<0.001
Vessels in macula		1.320(1.236-1.411)	<0.001		1.118(1.044-1.198)	0.0021
Vesel Area Density						
Vessels		0.694(0.647-0.745)	<0.001		0.880(0.813-0.953)	0.0021
Arteries		0.638(0.593-0.686)	<0.001		0.845(0.778-0.917)	<0.001
Arteries in macula		0.661(0.616-0.710)	<0.001		0.858(0.793-0.927)	<0.001
Arteries outside macula		0.658(0.611-0.708)	<0.001		0.862(0.794-0.936)	<0.001
Vessel Skeleton Density						
Arteries		0.624(0.580-0.671)	<0.001		0.843(0.776-0.916)	<0.001
Arteries in macula		0.655(0.612-0.700)	<0.001		0.837(0.777-0.902)	<0.001
Arteries outside macula		0.635(0.590-0.684)	<0.001		0.854(0.785-0.929)	<0.001
Tortuosity						
Inflection Count Tortuosity						
Arteries		0.853(0.792-0.919)	<0.001		0.917(0.853-0.986)	0.0204

Notes: The Adjusted Model was adjusted for age, sex, systolic blood pressure, total cholesterol, HDL, HbA1c, smoking, BMI, and Indices of Multiple Deprivation at baseline. * False Discovery Rate method was used to adjust P values in both models at a level of 0.05. HDL indicates high-density lipoprotein; HbA1c, glycosylated hemoglobin; BMI, body mass index; HR, hazard ratio, and CI, Confidence Interval.

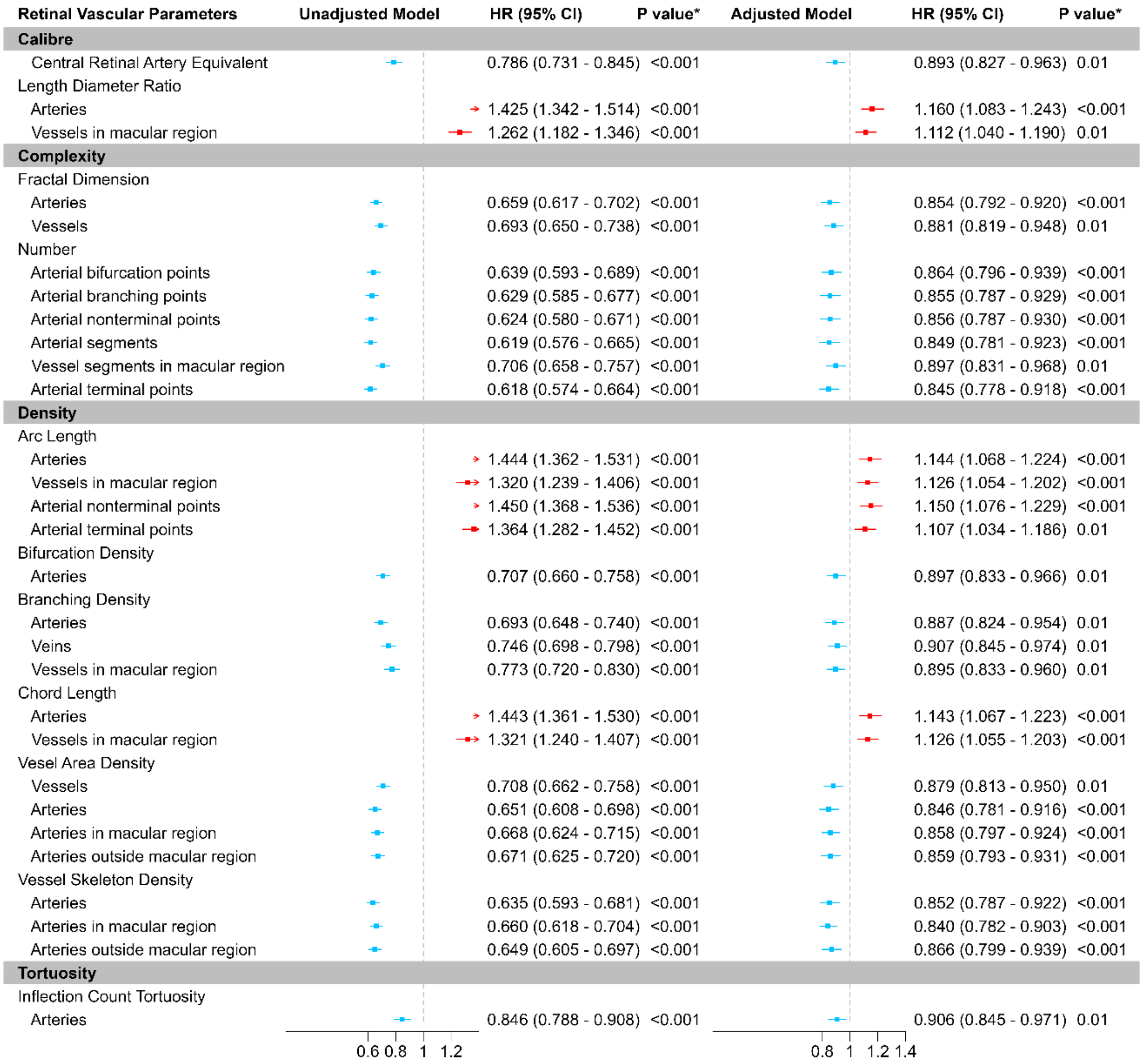
B. sensitivity analysis wherein individuals with cardiovascular disease risk were kept (N= 46775)



Retinal Vascular Parameters	Unadjusted Model	HR (95% CI)	P value*	Adjusted Model	HR (95% CI)	P value*
Calibre						
Central Retinal Artery Equivalent		0.993 (0.928 - 1.062)	0.83		0.981 (0.921 - 1.044)	0.54
Length Diameter Ratio						
Arteries		1.343 (1.281 - 1.409)	<0.001		1.115 (1.050 - 1.184)	0.01
Vessels in macular region		1.214 (1.150 - 1.282)	<0.001		1.079 (1.017 - 1.145)	0.02
Complexity						
Fractal Dimension						
Arteries		0.674 (0.635 - 0.716)	<0.001		0.882 (0.823 - 0.946)	0.01
Vessels		0.707 (0.666 - 0.750)	<0.001		0.910 (0.850 - 0.975)	0.01
Number						
Arterial bifurcation points		0.643 (0.600 - 0.689)	<0.001		0.869 (0.805 - 0.938)	0.01
Arterial branching points		0.644 (0.601 - 0.689)	<0.001		0.880 (0.815 - 0.950)	0.01
Arterial nonterminal points		0.633 (0.592 - 0.677)	<0.001		0.874 (0.809 - 0.944)	0.01
Arterial segments		0.629 (0.588 - 0.672)	<0.001		0.867 (0.802 - 0.936)	0.01
Vessel segments in macular region		0.713 (0.667 - 0.761)	<0.001		0.914 (0.852 - 0.981)	0.02
Arterial terminal points		0.627 (0.587 - 0.671)	<0.001		0.862 (0.798 - 0.931)	0.01
Density						
Arc Length						
Arteries		1.379 (1.313 - 1.448)	<0.001		1.115 (1.049 - 1.185)	0.01
Vessels in macular region		1.244 (1.185 - 1.305)	<0.001		1.092 (1.031 - 1.156)	0.01
Arterial nonterminal points		1.359 (1.298 - 1.423)	<0.001		1.117 (1.053 - 1.185)	0.01
Arterial terminal points		1.310 (1.244 - 1.380)	<0.001		1.079 (1.015 - 1.146)	0.02
Bifurcation Density						
Arteries		0.022 (0.011 - 0.045)	<0.001		0.333 (0.156 - 0.710)	0.01
Branching Density						
Arteries		0.051 (0.030 - 0.086)	<0.001		0.436 (0.245 - 0.777)	0.01
Veins		0.053 (0.026 - 0.106)	<0.001		0.502 (0.240 - 1.053)	0.07
Vessels in macular region		0.110 (0.064 - 0.190)	<0.001		0.378 (0.219 - 0.655)	0.01
Chord Length						
Arteries		1.381 (1.315 - 1.451)	<0.001		1.115 (1.049 - 1.185)	0.01
Vessels in macular region		1.221 (1.169 - 1.276)	<0.001		1.088 (1.028 - 1.151)	0.01
Vesel Area Density						
Vessels		0.727 (0.682 - 0.774)	<0.001		0.919 (0.856 - 0.986)	0.02
Arteries		0.668 (0.626 - 0.712)	<0.001		0.883 (0.821 - 0.951)	0.01
Arteries in macular region		0.681 (0.640 - 0.726)	<0.001		0.878 (0.819 - 0.941)	0.01
Arteries outside macular region		0.692 (0.648 - 0.738)	<0.001		0.903 (0.839 - 0.972)	0.01
Vessel Skeleton Density						
Arteries		0.647 (0.607 - 0.691)	<0.001		0.874 (0.811 - 0.941)	0.01
Arteries in macular region		0.669 (0.629 - 0.711)	<0.001		0.867 (0.810 - 0.929)	0.01
Arteries outside macular region		0.664 (0.622 - 0.709)	<0.001		0.892 (0.828 - 0.961)	0.01
Tortuosity						
Inflection Count Tortuosity						
Arteries		0.866 (0.811 - 0.925)	<0.001		0.929 (0.872 - 0.990)	0.03

Notes: The Adjusted Model was adjusted for age, sex, systolic blood pressure, total cholesterol, HDL, HbA1c, smoking, BMI, and Indices of Multiple Deprivation at baseline. * False Discovery Rate method was used to adjust P values in both models at a level of 0.05. HDL indicates high-density lipoprotein; HbA1c, glycosylated hemoglobin; BMI, body mass index; HR, hazard ratio, and CI, Confidence Interval.

C. sensitivity analysis accounting for spherical equivalent refractive error (N=45161)



Retinal Vascular Parameters	Unadjusted Model	HR (95% CI)	P value*	Adjusted Model	HR (95% CI)	P value*
Calibre						
Central Retinal Artery Equivalent		0.786 (0.731 - 0.845)	<0.001		0.893 (0.827 - 0.963)	0.01
Length Diameter Ratio						
Arteries		1.425 (1.342 - 1.514)	<0.001		1.160 (1.083 - 1.243)	<0.001
Vessels in macular region		1.262 (1.182 - 1.346)	<0.001		1.112 (1.040 - 1.190)	0.01
Complexity						
Fractal Dimension						
Arteries		0.659 (0.617 - 0.702)	<0.001		0.854 (0.792 - 0.920)	<0.001
Vessels		0.693 (0.650 - 0.738)	<0.001		0.881 (0.819 - 0.948)	0.01
Number						
Arterial bifurcation points		0.639 (0.593 - 0.689)	<0.001		0.864 (0.796 - 0.939)	<0.001
Arterial branching points		0.629 (0.585 - 0.677)	<0.001		0.855 (0.787 - 0.929)	<0.001
Arterial nonterminal points		0.624 (0.580 - 0.671)	<0.001		0.856 (0.787 - 0.930)	<0.001
Arterial segments		0.619 (0.576 - 0.665)	<0.001		0.849 (0.781 - 0.923)	<0.001
Vessel segments in macular region		0.706 (0.658 - 0.757)	<0.001		0.897 (0.831 - 0.968)	0.01
Arterial terminal points		0.618 (0.574 - 0.664)	<0.001		0.845 (0.778 - 0.918)	<0.001
Density						
Arc Length						
Arteries		1.444 (1.362 - 1.531)	<0.001		1.144 (1.068 - 1.224)	<0.001
Vessels in macular region		1.320 (1.239 - 1.406)	<0.001		1.126 (1.054 - 1.202)	<0.001
Arterial nonterminal points		1.450 (1.368 - 1.536)	<0.001		1.150 (1.076 - 1.229)	<0.001
Arterial terminal points		1.364 (1.282 - 1.452)	<0.001		1.107 (1.034 - 1.186)	0.01
Bifurcation Density						
Arteries		0.707 (0.660 - 0.758)	<0.001		0.897 (0.833 - 0.966)	0.01
Branching Density						
Arteries		0.693 (0.648 - 0.740)	<0.001		0.887 (0.824 - 0.954)	0.01
Veins		0.746 (0.698 - 0.798)	<0.001		0.907 (0.845 - 0.974)	0.01
Vessels in macular region		0.773 (0.720 - 0.830)	<0.001		0.895 (0.833 - 0.960)	0.01
Chord Length						
Arteries		1.443 (1.361 - 1.530)	<0.001		1.143 (1.067 - 1.223)	<0.001
Vessels in macular region		1.321 (1.240 - 1.407)	<0.001		1.126 (1.055 - 1.203)	<0.001
Vesel Area Density						
Vessels		0.708 (0.662 - 0.758)	<0.001		0.879 (0.813 - 0.950)	0.01
Arteries		0.651 (0.608 - 0.698)	<0.001		0.846 (0.781 - 0.916)	<0.001
Arteries in macular region		0.668 (0.624 - 0.715)	<0.001		0.858 (0.797 - 0.924)	<0.001
Arteries outside macular region		0.671 (0.625 - 0.720)	<0.001		0.859 (0.793 - 0.931)	<0.001
Vessel Skeleton Density						
Arteries		0.635 (0.593 - 0.681)	<0.001		0.852 (0.787 - 0.922)	<0.001
Arteries in macular region		0.660 (0.618 - 0.704)	<0.001		0.840 (0.782 - 0.903)	<0.001
Arteries outside macular region		0.649 (0.605 - 0.697)	<0.001		0.866 (0.799 - 0.939)	<0.001
Tortuosity						
Inflection Count Tortuosity						
Arteries		0.846 (0.788 - 0.908)	<0.001		0.906 (0.845 - 0.971)	0.01

Notes: Notes: The Adjusted Model was adjusted for age, sex, systolic blood pressure, total cholesterol, HDL, HbA1c, smoking, BMI, and Indices of Multiple Deprivation, and spherical equivalent refractive error at baseline * The False Discovery Rate method was used to adjust P values at a level of 0.05. HR, hazard ratio, and CI, Confidence Interval. HR represents the relative risk of incident stroke for each 1 standard deviation increase in the exposure.

Supplementary Table 5. Retinal vascular parameters and incident stroke risk stratified by age group at baseline using the Cox proportional hazard model.

Variables	P for interaction	Younger		Older	
		HR (95%CI)	P for association	HR (95%CI)	P for association
Central Retinal Artery Equivalent	0.572	0.830 (0.707 - 0.975)	0.023	0.896 (0.824 - 0.975)	0.011
Length Diameter Ratio (artery)	0.885	1.212 (1.028 - 1.428)	0.022	1.205 (1.122 - 1.295)	<0.001
Length Diameter Ratio in macula	0.772	1.125 (0.957 - 1.321)	0.153	1.142 (1.061 - 1.228)	<0.001
Fractal Dimension (artery)	0.492	0.828 (0.705 - 0.973)	0.022	0.792 (0.731 - 0.858)	<0.001
Fractal Dimension (vessel)	0.675	0.841 (0.716 - 0.989)	0.036	0.825 (0.764 - 0.892)	<0.001
Number of bifurcation points (artery)	0.81	0.799 (0.680 - 0.939)	0.007	0.793 (0.723 - 0.869)	<0.001
Number of branching points (artery)	0.499	0.815 (0.693 - 0.959)	0.013	0.777 (0.709 - 0.851)	<0.001
Number of vessel segments (artery)	0.297	0.835 (0.710 - 0.983)	0.031	0.768 (0.700 - 0.842)	<0.001
Number of vessel segments (macula)	0.43	0.811 (0.690 - 0.954)	0.011	0.765 (0.698 - 0.839)	<0.001
Number of nonterminal (artery)	0.641	0.867 (0.739 - 1.018)	0.082	0.838 (0.771 - 0.911)	<0.001
Number of terminal (artery)	0.619	0.790 (0.672 - 0.927)	0.004	0.766 (0.699 - 0.840)	<0.001
Arc length (artery)	0.616	1.181 (0.998 - 1.397)	0.053	1.221 (1.137 - 1.310)	<0.001
Arc length in macula	0.436	1.110 (0.940 - 1.311)	0.218	1.183 (1.102 - 1.269)	<0.001
Arc length of nonterminal (artery)	0.431	1.160 (0.978 - 1.377)	0.088	1.233 (1.151 - 1.322)	<0.001
Arc length of terminal (artery)	0.987	1.169 (0.990 - 1.381)	0.065	1.159 (1.078 - 1.247)	<0.001
Bifurcation density (artery)	0.67	0.865 (0.734 - 1.021)	0.087	0.842 (0.777 - 0.912)	<0.001
Branching density (artery)	0.74	0.806 (0.685 - 0.947)	0.009	0.840 (0.776 - 0.910)	<0.001
Branching density (vein)	0.678	0.828 (0.704 - 0.975)	0.023	0.870 (0.805 - 0.940)	<0.001
Branching density in macula	0.115	0.963 (0.818 - 1.135)	0.654	0.840 (0.776 - 0.909)	<0.001
Chord length (artery)	0.538	1.168 (0.986 - 1.384)	0.073	1.221 (1.138 - 1.311)	<0.001
Chord length in macula	0.391	1.103 (0.933 - 1.304)	0.25	1.184 (1.104 - 1.271)	<0.001

Vessel Area Density	0.626	0.856 (0.729 - 1.004)	0.056	0.839 (0.772 - 0.912)	<0.001
Vessel Area Density (artery)	0.43	0.829 (0.706 - 0.975)	0.024	0.788 (0.722 - 0.858)	<0.001
Vessel Area Density (artery) in macula	0.522	0.839 (0.713 - 0.988)	0.036	0.798 (0.735 - 0.865)	<0.001
Vessel Area Density (artery) outside macula	0.48	0.842 (0.717 - 0.989)	0.036	0.807 (0.740 - 0.880)	<0.001
Vessel Skeleton Density (artery)	0.302	0.835 (0.710 - 0.981)	0.028	0.769 (0.705 - 0.838)	<0.001
Vessel Skeleton Density (artery) in macula	0.456	0.825 (0.704 - 0.968)	0.018	0.775 (0.717 - 0.838)	<0.001
Vessel Skeleton Density (artery) outside macula	0.367	0.841 (0.716 - 0.987)	0.034	0.786 (0.719 - 0.859)	<0.001
Inflection count tortuosity (artery)	0.666	0.916 (0.778 - 1.077)	0.288	0.885 (0.819 - 0.956)	0.002

Notes: Participants were divided into younger and older groups by mean age. Model adjusted for sex, hypertension, smoke group, total cholesterol, high-density lipoprotein, obesity, Indices of Multiple Deprivation, and diabetes.

Supplementary Table 6. Retinal vascular parameters and incident stroke risk stratified by gender group at baseline using the Cox proportional hazard model.

Variables	P for interaction	Male		Female	
		HR (95%CI)	P for association	HR (95%CI)	P for association
Central Retinal Artery Equivalent	0.401	0.906 (0.819 - 1.002)	0.054	0.856 (0.766 - 0.956)	0.006
Length Diameter Ratio (artery)	0.967	1.215 (1.111 - 1.328)	<0.001	1.196 (1.085 - 1.319)	<0.001
Length Diameter Ratio in macula	0.05	1.213 (1.110 - 1.326)	<0.001	1.050 (0.949 - 1.162)	0.341
Fractal Dimension (artery)	0.304	0.823 (0.747 - 0.906)	<0.001	0.772 (0.694 - 0.859)	<0.001
Fractal Dimension (vessel)	0.303	0.855 (0.777 - 0.940)	0.001	0.800 (0.722 - 0.887)	<0.001
Number of bifurcation points (artery)	0.635	0.803 (0.722 - 0.894)	<0.001	0.786 (0.696 - 0.886)	<0.001
Number of branching points (artery)	0.614	0.797 (0.716 - 0.887)	<0.001	0.776 (0.688 - 0.874)	<0.001
Number of vessel segments (artery)	0.396	0.805 (0.723 - 0.896)	<0.001	0.762 (0.676 - 0.858)	<0.001
Number of vessel segments (macula)	0.453	0.794 (0.713 - 0.883)	<0.001	0.758 (0.672 - 0.854)	<0.001
Number of nonterminal (artery)	0.892	0.845 (0.765 - 0.934)	<0.001	0.846 (0.758 - 0.946)	0.003
Number of terminal (artery)	0.538	0.785 (0.706 - 0.873)	<0.001	0.758 (0.672 - 0.855)	<0.001
Arc length (artery)	0.656	1.203 (1.101 - 1.314)	<0.001	1.227 (1.114 - 1.351)	<0.001
Arc length in macula	0.09	1.235 (1.133 - 1.345)	<0.001	1.090 (0.987 - 1.204)	0.09
Arc length of nonterminal (artery)	0.283	1.187 (1.087 - 1.296)	<0.001	1.263 (1.150 - 1.388)	<0.001
Arc length of terminal (artery)	0.68	1.182 (1.080 - 1.293)	<0.001	1.138 (1.031 - 1.255)	0.01
Bifurcation density (artery)	0.873	0.838 (0.760 - 0.925)	<0.001	0.857 (0.771 - 0.953)	0.004
Branching density (artery)	0.871	0.835 (0.758 - 0.919)	<0.001	0.834 (0.750 - 0.928)	<0.001
Branching density (vein)	0.836	0.867 (0.788 - 0.953)	0.003	0.860 (0.775 - 0.954)	0.004
Branching density in macula	0.148	0.819 (0.744 - 0.902)	<0.001	0.919 (0.828 - 1.020)	0.113
Chord length (artery)	0.656	1.202 (1.100 - 1.313)	<0.001	1.226 (1.113 - 1.349)	<0.001
Chord length in macula	0.083	1.236 (1.135 - 1.347)	<0.001	1.089 (0.986 - 1.203)	0.093

Vessel Area Density	0.566	0.857 (0.776 - 0.947)	0.002	0.828 (0.743 - 0.924)	<0.001
Vessel Area Density (artery)	0.495	0.812 (0.733 - 0.900)	<0.001	0.781 (0.697 - 0.875)	<0.001
Vessel Area Density (artery) in macula	0.848	0.808 (0.732 - 0.892)	<0.001	0.806 (0.724 - 0.898)	<0.001
Vessel Area Density (artery) outside macula	0.37	0.837 (0.755 - 0.928)	<0.001	0.791 (0.705 - 0.886)	<0.001
Vessel Skeleton Density (artery)	0.239	0.813 (0.734 - 0.900)	<0.001	0.750 (0.669 - 0.841)	<0.001
Vessel Skeleton Density (artery) in macula	0.438	0.802 (0.731 - 0.881)	<0.001	0.767 (0.691 - 0.851)	<0.001
Vessel Skeleton Density (artery) outside macula	0.191	0.833 (0.751 - 0.925)	<0.001	0.760 (0.676 - 0.853)	<0.001
Inflection count tortuosity (artery)	0.034	0.955 (0.868 - 1.051)	0.347	0.823 (0.744 - 0.912)	<0.001

Notes: Model adjusted for age group, hypertension, smoke group, total cholesterol, high-density lipoprotein, obesity, Indices of Multiple Deprivation, and diabetes.

Supplementary Table 7. Retinal vascular parameters and incident stroke risk stratified by smoking status at baseline using the Cox proportional hazard model.

Variables	P for interaction	No		Yes	
		HR (95%CI)	P for association	HR (95%CI)	P for association
Central Retinal Artery Equivalent	0.457	0.914 (0.822 - 1.015)	0.093	0.853 (0.767 - 0.947)	0.003
Length Diameter Ratio (artery)	0.356	1.229 (1.122 - 1.347)	<0.001	1.183 (1.077 - 1.301)	<0.001
Length Diameter Ratio in macula	0.994	1.129 (1.028 - 1.240)	0.011	1.149 (1.045 - 1.263)	0.004
Fractal Dimension (artery)	0.661	0.800 (0.723 - 0.885)	<0.001	0.800 (0.723 - 0.885)	<0.001
Fractal Dimension (vessel)	0.436	0.818 (0.741 - 0.903)	<0.001	0.840 (0.761 - 0.928)	<0.001
Number of bifurcation points (artery)	0.699	0.798 (0.713 - 0.893)	<0.001	0.793 (0.708 - 0.889)	<0.001
Number of branching points (artery)	0.383	0.774 (0.692 - 0.866)	<0.001	0.800 (0.714 - 0.895)	<0.001
Number of vessel segments (artery)	0.22	0.761 (0.680 - 0.851)	<0.001	0.810 (0.723 - 0.907)	<0.001
Number of vessel segments (macula)	0.361	0.764 (0.683 - 0.855)	<0.001	0.791 (0.706 - 0.885)	<0.001
Number of nonterminal (artery)	0.27	0.822 (0.740 - 0.912)	<0.001	0.869 (0.782 - 0.965)	0.009
Number of terminal (artery)	0.587	0.772 (0.690 - 0.863)	<0.001	0.774 (0.691 - 0.866)	<0.001
Arc length (artery)	0.098	1.266 (1.157 - 1.386)	<0.001	1.163 (1.059 - 1.278)	0.002
Arc length in macula	0.58	1.181 (1.078 - 1.295)	<0.001	1.160 (1.058 - 1.272)	0.002
Arc length of nonterminal (artery)	0.129	1.267 (1.159 - 1.385)	<0.001	1.178 (1.074 - 1.292)	<0.001
Arc length of terminal (artery)	0.103	1.214 (1.107 - 1.331)	<0.001	1.108 (1.006 - 1.220)	0.037
Bifurcation density (artery)	0.058	0.799 (0.722 - 0.885)	<0.001	0.897 (0.810 - 0.995)	0.039
Branching density (artery)	0.574	0.828 (0.749 - 0.916)	<0.001	0.840 (0.758 - 0.929)	<0.001
Branching density (vein)	0.023	0.804 (0.729 - 0.887)	<0.001	0.928 (0.839 - 1.026)	0.144
Branching density in macula	0.627	0.855 (0.774 - 0.945)	0.002	0.870 (0.787 - 0.962)	0.007
Chord length (artery)	0.102	1.264 (1.155 - 1.384)	<0.001	1.162 (1.058 - 1.277)	0.002
Chord length in macula	0.57	1.183 (1.079 - 1.296)	<0.001	1.160 (1.058 - 1.271)	0.002

Vessel Area Density	0.824	0.848 (0.765 - 0.941)	0.002	0.839 (0.756 - 0.931)	<0.001
Vessel Area Density (artery)	0.933	0.814 (0.732 - 0.906)	<0.001	0.781 (0.701 - 0.870)	<0.001
Vessel Area Density (artery) in macula	0.58	0.801 (0.723 - 0.888)	<0.001	0.812 (0.732 - 0.900)	<0.001
Vessel Area Density (artery) outside macula	0.957	0.830 (0.746 - 0.925)	<0.001	0.801 (0.718 - 0.892)	<0.001
Vessel Skeleton Density (artery)	0.676	0.786 (0.706 - 0.875)	<0.001	0.782 (0.702 - 0.871)	<0.001
Vessel Skeleton Density (artery) in macula	0.368	0.771 (0.699 - 0.850)	<0.001	0.801 (0.726 - 0.884)	<0.001
Vessel Skeleton Density (artery) outside macula	0.842	0.808 (0.725 - 0.902)	<0.001	0.791 (0.708 - 0.882)	<0.001
Inflection count tortuosity (artery)	0.126	0.848 (0.769 - 0.935)	<0.001	0.937 (0.849 - 1.035)	0.201

Notes: Participants were divided into smoker (yes [current, previous]) and non-smoker (no [never]) groups. Model adjusted for sex, hypertension, age group, total cholesterol, high-density lipoprotein, obesity, Indices of Multiple Deprivation, and diabetes.

Supplementary Table 8. Retinal vascular parameters and incident stroke risk stratified by the presence of obesity at baseline using the Cox proportional hazard model.

Variables	P for interaction	No		Yes	
		HR (95%CI)	P for association	HR (95%CI)	P for association
Central Retinal Artery Equivalent	0.248	0.866 (0.793 - 0.945)	0.001	0.931 (0.808 - 1.073)	0.325
Length Diameter Ratio (artery)	0.756	1.205 (1.115 - 1.301)	<0.001	1.212 (1.069 - 1.375)	0.003
Length Diameter Ratio in macula	0.869	1.130 (1.045 - 1.222)	0.002	1.160 (1.022 - 1.316)	0.021
Fractal Dimension (artery)	0.114	0.778 (0.716 - 0.845)	<0.001	0.858 (0.744 - 0.988)	0.034
Fractal Dimension (vessel)	0.113	0.806 (0.743 - 0.874)	<0.001	0.891 (0.776 - 1.023)	0.101
Number of bifurcation points (artery)	0.672	0.794 (0.723 - 0.871)	<0.001	0.795 (0.681 - 0.929)	0.004
Number of branching points (artery)	0.122	0.763 (0.695 - 0.837)	<0.001	0.852 (0.730 - 0.995)	0.043
Number of vessel segments (artery)	0.271	0.770 (0.701 - 0.845)	<0.001	0.822 (0.704 - 0.961)	0.014
Number of vessel segments (macula)	0.204	0.759 (0.692 - 0.833)	<0.001	0.824 (0.705 - 0.963)	0.015
Number of nonterminal (artery)	0.904	0.852 (0.781 - 0.929)	<0.001	0.823 (0.713 - 0.949)	0.007
Number of terminal (artery)	0.148	0.751 (0.685 - 0.824)	<0.001	0.829 (0.710 - 0.968)	0.018
Arc length (artery)	0.627	1.219 (1.129 - 1.316)	<0.001	1.209 (1.067 - 1.370)	0.003
Arc length in macula	0.886	1.170 (1.084 - 1.262)	<0.001	1.174 (1.037 - 1.329)	0.011
Arc length of nonterminal (artery)	0.732	1.223 (1.134 - 1.318)	<0.001	1.226 (1.085 - 1.386)	0.001
Arc length of terminal (artery)	0.671	1.165 (1.078 - 1.259)	<0.001	1.154 (1.015 - 1.311)	0.028
Bifurcation density (artery)	0.345	0.834 (0.766 - 0.907)	<0.001	0.879 (0.764 - 1.012)	0.072
Branching density (artery)	0.612	0.830 (0.763 - 0.902)	<0.001	0.843 (0.736 - 0.966)	0.014
Branching density (vein)	0.147	0.838 (0.772 - 0.910)	<0.001	0.929 (0.811 - 1.065)	0.291
Branching density in macula	0.226	0.842 (0.774 - 0.915)	<0.001	0.917 (0.801 - 1.049)	0.205
Chord length (artery)	0.562	1.220 (1.130 - 1.317)	<0.001	1.200 (1.059 - 1.361)	0.004
Chord length in macula	0.819	1.172 (1.086 - 1.265)	<0.001	1.169 (1.033 - 1.323)	0.014

Vessel Area Density	0.086	0.817 (0.750 - 0.890)	<0.001	0.918 (0.795 - 1.060)	0.245
Vessel Area Density (artery)	0.105	0.775 (0.709 - 0.846)	<0.001	0.861 (0.741 - 1.001)	0.051
Vessel Area Density (artery) in macula	0.997	0.812 (0.746 - 0.883)	<0.001	0.789 (0.685 - 0.909)	0.001
Vessel Area Density (artery) outside macula	0.055	0.787 (0.720 - 0.860)	<0.001	0.899 (0.774 - 1.045)	0.167
Vessel Skeleton Density (artery)	0.118	0.761 (0.696 - 0.831)	<0.001	0.844 (0.727 - 0.980)	0.027
Vessel Skeleton Density (artery) in macula	0.982	0.790 (0.728 - 0.857)	<0.001	0.769 (0.673 - 0.880)	<0.001
Vessel Skeleton Density (artery) outside macula	0.034	0.765 (0.699 - 0.837)	<0.001	0.896 (0.770 - 1.043)	0.158
Inflection count tortuosity (artery)	0.63	0.902 (0.831 - 0.979)	0.014	0.862 (0.755 - 0.984)	0.028

Notes: Obesity was defined as a body mass index of greater than or equal to 30. Model adjusted for sex, hypertension, smoke group, total cholesterol, high-density lipoprotein, age group, Indices of Multiple Deprivation, and diabetes.

Supplementary Table 9. Retinal vascular parameters and incident stroke risk stratified by the presence of diabetes at baseline using the Cox proportional hazard model.

Variables	P for interaction	No		Yes	
		HR (95%CI)	P for association	HR (95%CI)	P for association
Central Retinal Artery Equivalent	0.726	0.882 (0.815 - 0.954)	0.002	0.903 (0.707 - 1.153)	0.412
Length Diameter Ratio (artery)	0.725	1.206 (1.125 - 1.292)	<0.001	1.228 (0.988 - 1.527)	0.064
Length Diameter Ratio in macula	0.862	1.138 (1.061 - 1.221)	<0.001	1.148 (0.922 - 1.430)	0.217
Fractal Dimension (artery)	0.762	0.807 (0.749 - 0.870)	<0.001	0.721 (0.569 - 0.914)	0.007
Fractal Dimension (vessel)	0.921	0.834 (0.775 - 0.898)	<0.001	0.766 (0.610 - 0.963)	0.022
Number of bifurcation points (artery)	0.825	0.797 (0.733 - 0.867)	<0.001	0.772 (0.594 - 1.002)	0.051
Number of branching points (artery)	0.84	0.789 (0.726 - 0.858)	<0.001	0.752 (0.577 - 0.982)	0.036
Number of vessel segments (artery)	0.971	0.789 (0.726 - 0.858)	<0.001	0.730 (0.558 - 0.956)	0.022
Number of vessel segments (macula)	0.942	0.781 (0.718 - 0.849)	<0.001	0.728 (0.557 - 0.951)	0.02
Number of nonterminal (artery)	0.651	0.853 (0.789 - 0.922)	<0.001	0.759 (0.598 - 0.965)	0.024
Number of terminal (artery)	0.911	0.776 (0.714 - 0.844)	<0.001	0.730 (0.560 - 0.952)	0.02
Arc length (artery)	0.754	1.213 (1.133 - 1.299)	<0.001	1.243 (1.001 - 1.543)	0.049
Arc length in macula	0.575	1.175 (1.098 - 1.258)	<0.001	1.137 (0.917 - 1.409)	0.241
Arc length of nonterminal (artery)	0.978	1.217 (1.138 - 1.302)	<0.001	1.284 (1.042 - 1.581)	0.019
Arc length of terminal (artery)	0.6	1.163 (1.085 - 1.248)	<0.001	1.151 (0.926 - 1.429)	0.205
Bifurcation density (artery)	0.589	0.845 (0.783 - 0.911)	<0.001	0.854 (0.674 - 1.083)	0.193
Branching density (artery)	0.755	0.834 (0.774 - 0.899)	<0.001	0.826 (0.654 - 1.043)	0.108
Branching density (vein)	0.319	0.856 (0.795 - 0.921)	<0.001	0.934 (0.739 - 1.180)	0.564
Branching density in macula	0.676	0.868 (0.806 - 0.936)	<0.001	0.802 (0.636 - 1.012)	0.063
Chord length (artery)	0.745	1.212 (1.132 - 1.298)	<0.001	1.241 (0.999 - 1.541)	0.051
Chord length in macula	0.606	1.175 (1.097 - 1.258)	<0.001	1.143 (0.922 - 1.416)	0.222

Vessel Area Density	0.692	0.852 (0.789 - 0.921)	<0.001	0.753 (0.589 - 0.962)	0.023
Vessel Area Density (artery)	0.782	0.805 (0.743 - 0.872)	<0.001	0.718 (0.556 - 0.927)	0.011
Vessel Area Density (artery) in macula	0.507	0.803 (0.744 - 0.867)	<0.001	0.837 (0.661 - 1.061)	0.141
Vessel Area Density (artery) outside macula	0.626	0.825 (0.762 - 0.894)	<0.001	0.714 (0.551 - 0.924)	0.01
Vessel Skeleton Density (artery)	0.925	0.789 (0.729 - 0.855)	<0.001	0.722 (0.560 - 0.931)	0.012
Vessel Skeleton Density (artery) in macula	0.721	0.785 (0.730 - 0.845)	<0.001	0.783 (0.626 - 0.980)	0.032
Vessel Skeleton Density (artery) outside macula	0.93	0.805 (0.742 - 0.873)	<0.001	0.734 (0.565 - 0.952)	0.02
Inflection count tortuosity (artery)	0.034	0.871 (0.810 - 0.937)	<0.001	1.111 (0.880 - 1.403)	0.374

Notes: Model adjusted for sex, hypertension, smoke group, total cholesterol, high-density lipoprotein, obesity, Indices of Multiple Deprivation, and age group.

Supplementary Table 10. Retinal vascular parameters and incident stroke risk stratified by the presence of hypertension at baseline using the Cox proportional hazard model.

Variables	P for interaction	No		Yes	
		HR (95%CI)	P for association	HR (95%CI)	P for association
Central Retinal Artery Equivalent	0.966	0.883 (0.787 - 0.991)	0.035	0.884 (0.801 - 0.975)	0.013
Length Diameter Ratio (artery)	0.05	1.102 (0.982 - 1.237)	0.099	1.263 (1.165 - 1.369)	<0.001
Length Diameter Ratio in macula	0.224	1.082 (0.967 - 1.210)	0.168	1.170 (1.077 - 1.272)	<0.001
Fractal Dimension (artery)	0.314	0.834 (0.743 - 0.936)	0.002	0.778 (0.710 - 0.853)	<0.001
Fractal Dimension (vessel)	0.168	0.876 (0.781 - 0.981)	0.022	0.800 (0.732 - 0.875)	<0.001
Number of bifurcation points (artery)	0.333	0.827 (0.733 - 0.934)	0.002	0.771 (0.693 - 0.858)	<0.001
Number of branching points (artery)	0.074	0.850 (0.752 - 0.959)	0.009	0.741 (0.667 - 0.824)	<0.001
Number of vessel segments (artery)	0.055	0.854 (0.755 - 0.965)	0.011	0.736 (0.661 - 0.818)	<0.001
Number of vessel segments (macula)	0.086	0.837 (0.741 - 0.945)	0.004	0.734 (0.660 - 0.816)	<0.001
Number of nonterminal (artery)	0.085	0.910 (0.810 - 1.023)	0.114	0.802 (0.729 - 0.884)	<0.001
Number of terminal (artery)	0.142	0.822 (0.728 - 0.928)	0.002	0.736 (0.662 - 0.819)	<0.001
Arc length (artery)	0.045	1.111 (0.991 - 1.245)	0.07	1.273 (1.175 - 1.379)	<0.001
Arc length in macula	0.496	1.141 (1.025 - 1.271)	0.016	1.186 (1.093 - 1.287)	<0.001
Arc length of nonterminal (artery)	0.138	1.146 (1.025 - 1.282)	0.017	1.263 (1.167 - 1.366)	<0.001
Arc length of terminal (artery)	0.01	1.032 (0.920 - 1.158)	0.589	1.237 (1.139 - 1.342)	<0.001
Bifurcation density (artery)	0.157	0.899 (0.800 - 1.010)	0.074	0.815 (0.743 - 0.894)	<0.001
Branching density (artery)	0.016	0.931 (0.828 - 1.046)	0.227	0.780 (0.712 - 0.854)	<0.001
Branching density (vein)	0.482	0.883 (0.789 - 0.989)	0.031	0.850 (0.777 - 0.929)	<0.001
Branching density in macula	0.586	0.880 (0.785 - 0.987)	0.029	0.853 (0.779 - 0.933)	<0.001
Chord length (artery)	0.041	1.107 (0.988 - 1.241)	0.08	1.272 (1.175 - 1.378)	<0.001

Chord length in macula	0.497	1.141 (1.025 - 1.271)	0.016	1.187 (1.094 - 1.288)	<0.001
Vessel Area Density	0.198	0.888 (0.791 - 0.997)	0.044	0.814 (0.740 - 0.896)	<0.001
Vessel Area Density (artery)	0.235	0.839 (0.746 - 0.944)	0.003	0.769 (0.696 - 0.850)	<0.001
Vessel Area Density (artery) in macula	0.244	0.850 (0.758 - 0.952)	0.005	0.777 (0.707 - 0.855)	<0.001
Vessel Area Density (artery) outside macula	0.256	0.855 (0.760 - 0.962)	0.009	0.788 (0.713 - 0.871)	<0.001
Vessel Skeleton Density (artery)	0.245	0.822 (0.731 - 0.926)	0.001	0.756 (0.684 - 0.836)	<0.001
Vessel Skeleton Density (artery) in macula	0.524	0.807 (0.723 - 0.900)	<0.001	0.771 (0.704 - 0.844)	<0.001
Vessel Skeleton Density (artery) outside macula	0.269	0.835 (0.741 - 0.942)	0.003	0.773 (0.698 - 0.856)	<0.001
Inflection count tortuosity (artery)	0.302	0.932 (0.832 - 1.043)	0.22	0.867 (0.793 - 0.947)	0.002

Notes: Hypertension was defined as a systolic blood pressure of greater than or equal to 140 or a diastolic blood pressure of greater than or equal to 90. Model adjusted for sex, age group, smoke group, total cholesterol, high-density lipoprotein, obesity, Indices of Multiple Deprivation, and diabetes.

Supplementary Table 11. Parameters generated by Retina-Based Microvascular Health Assessment System

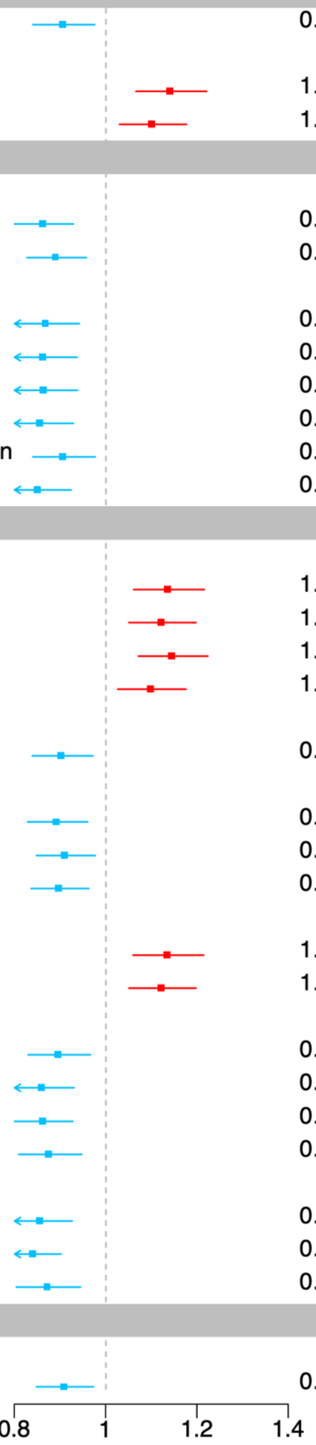
Category	**Measure type**	**Parameter**
Branching Angle	Angular Asymmetry	Angular Asymmetry(edge)(artery)
Branching Angle	Angular Asymmetry	Angular Asymmetry(edge)(vein)
Branching Angle	Angular Asymmetry	Angular Asymmetry(edge)-macula
Branching Angle	Angular Asymmetry	Angular Asymmetry(artery)
Branching Angle	Angular Asymmetry	Angular Asymmetry(vein)
Branching Angle	Angular Asymmetry	Angular Asymmetry-macula
Branching Angle	Asymmetry Ratio	Asymmetry Ratio(artery)
Branching Angle	Asymmetry Ratio	Asymmetry Ratio(vein)
Branching Angle	Asymmetry Ratio	Asymmetry Ratio-macula
Branching Angle	Branching Angle	Branching Angle(edge)(artery)
Branching Angle	Branching Angle	Branching Angle(edge)(vein)
Branching Angle	Branching Angle	Branching Angle(edge)-macula
Branching Angle	Branching Angle	Branching Angle(artery)
Branching Angle	Branching Angle	Branching Angle(vein)
Branching Angle	Branching Angle	Branching Angle-macula
Branching Angle	Branching Coefficient	Branching Coefficient(artery)
Branching Angle	Branching Coefficient	Branching Coefficient(vein)
Branching Angle	Branching Coefficient	Branching Coefficient-macula
Branching Angle	Junctional Exponent Deviation	Junctional Exponent Deviation(artery)
Branching Angle	Junctional Exponent Deviation	Junctional Exponent Deviation(vein)
Branching Angle	Junctional Exponent Deviation	Junctional Exponent Deviation-macula

Calibre	Artery-to-Vein Ratio	Artery-to-Vein Ratio (from equivalents)
Calibre	Central Retinal Artery Equivalent	Central Retinal Artery Equivalent
Calibre	Central Retinal Vein Equivalent	Central Retinal Vein Equivalent
Calibre	Length Diameter Ratio	Length Diameter Ratio(artery)
Calibre	Length Diameter Ratio	Length Diameter Ratio(vein)
Calibre	Length Diameter Ratio	Length Diameter Ratio-macula
Calibre	Width	Calibre(artery)
Calibre	Width	Calibre(vein)
Calibre	Width	Calibre-macula
Calibre	Width	Calibre_nonterminal(artery)
Calibre	Width	Calibre_nonterminal(vein)
Calibre	Width	Calibre_terminal(artery)
Calibre	Width	Calibre_terminal(vein)
Complexity	Fractal Dimension	Dractal Dimension(artery)
Complexity	Fractal Dimension	Fractal Dimension(vessel)
Complexity	Fractal Dimension	Fractal Dimension(vein)
Complexity	Level	level(artery)
Complexity	Level	level(vein)
Complexity	Level	level-macula
Complexity	Number	Number of bifurcation points(artery)
Complexity	Number	Number of bifurcation points(vein)
Complexity	Number	Number of bifurcation points-macula
Complexity	Number	Number of branching points(artery)
Complexity	Number	Number of branching points(vein)
Complexity	Number	Number of branching points-macula
Complexity	Number	N_nonterminal(artery)
Complexity	Number	N_nonterminal(vein)
Complexity	Number	Number of vessel segments(artery)
Complexity	Number	Number of vessel segments(vein)
Complexity	Number	Number of vessel segments-macula
Complexity	Number	N_terminal(artery)
Complexity	Number	N_terminal(vein)
Complexity	Number	Number of vessel tree(artery)
Complexity	Number	Number of vessel tree(vein)
Complexity	Number	Number of vessel tree-macula
Complexity	Strahler	Strahler(artery)

Complexity	Strahler	Strahler(vein)
Complexity	Strahler	Strahler-macula
Density	Arc Length	Arc length(artery)
Density	Arc Length	Arc length(vein)
Density	Arc Length	Arc length-macula
Density	Arc Length	Arc length_nonterminal(artery)
Density	Arc Length	Arc length_nonterminal(vein)
Density	Arc Length	Arc length_terminal(artery)
Density	Arc Length	Arc length_terminal(vein)
Density	Bifurcation Density	Bifurcation density(artery)
Density	Bifurcation Density	Bifurcation density(vein)
Density	Bifurcation Density	Bifurcation density-macula
Density	Branching Density	Branching density(artery)
Density	Branching Density	Branching density(vein)
Density	Branching Density	Branching density-macula
Density	Chord Length	Chord length(artery)
Density	Chord Length	Chord length(vein)
Density	Chord Length	Chord length-macula
Density	Vessel Area Density	Vessel Area Density
Density	Vessel Area Density	Vessel Area Density(artery)
Density	Vessel Area Density	Vessel Area Density(artery)-macula
Density	Vessel Area Density	Vessel Area Density(artery)-other
Density	Vessel Area Density	Vessel Area Density(vein)
Density	Vessel Area Density	Vessel Area Density(vein)-macula
Density	Vessel Area Density	Vessel Area Density(vein)-other
Density	Vessel Skeleton Density	Vessel Skeleton Density(artery)
Density	Vessel Skeleton Density	Vessel Skeleton Density(artery)-macula
Density	Vessel Skeleton Density	Vessel Skeleton Density(artery)-other
Density	Vessel Skeleton Density	Vessel Skeleton Density(vein)
Density	Vessel Skeleton Density	Vessel Skeleton Density(vein)-macula
Density	Vessel Skeleton Density	Vessel Skeleton Density(vein)-other
Tortuosity	Turning Angles	Turning angles(artery)
Tortuosity	Turning Angles	Turning angles(vein)
Tortuosity	Turning Angles	Turning angles-macula
Tortuosity	Angle-based Tortuosity	Angle-based tortuosity(artery)
Tortuosity	Angle-based Tortuosity	Angle-based tortuosity(vein)
Tortuosity	Angle-based Tortuosity	Angle-based tortuosity-macula

Tortuosity	Curve Angle	Curve Angle(artery)
Tortuosity	Curve Angle	Curve Angle(vein)
Tortuosity	Curve Angle	Curve Angle-macula
Tortuosity	Squared Curvature Tortuosity	Squared curvature tortuosity(artery)
Tortuosity	Squared Curvature Tortuosity	Squared curvature tortuosity(vein)
Tortuosity	Squared Curvature Tortuosity	Squared curvature tortuosity-macula
Tortuosity	Fractal Tortuosity	Fractal tortuosity(artery)
Tortuosity	Fractal Tortuosity	Fractal tortuosity(vein)
Tortuosity	Fractal Tortuosity	Fractal tortuosity-macula
Tortuosity	Inflection Count Tortuosity	Inflection count tortuosity(artery)
Tortuosity	Inflection Count Tortuosity	Inflection count tortuosity(vein)
Tortuosity	Inflection Count Tortuosity	Inflection count tortuosity-macula
Tortuosity	Linear Regression Tortuosity	Linear regression tortuosity(artery)
Tortuosity	Linear Regression Tortuosity	Linear regression tortuosity(vein)
Tortuosity	Linear Regression Tortuosity	Linear regression tortuosity-macula
Tortuosity	Tortuosity Density	Tortuosity Density(artery)
Tortuosity	Tortuosity Density	Tortuosity Density(vein)
Tortuosity	Tortuosity Density	Tortuosity Density-macula
Tortuosity	Distance-based Tortuosity	Distance-based tortuosity(artery)
Tortuosity	Distance-based Tortuosity	Distance-based tortuosity(vein)
Tortuosity	Distance-based Tortuosity	Distance-based tortuosity-macula
Tortuosity	Twist-based Tortuosity	Twist-based tortuosity(artery)
Tortuosity	Twist-based Tortuosity	Twist-based tortuosity(vein)
Tortuosity	Twist-based Tortuosity	Twist-based tortuosity-macula

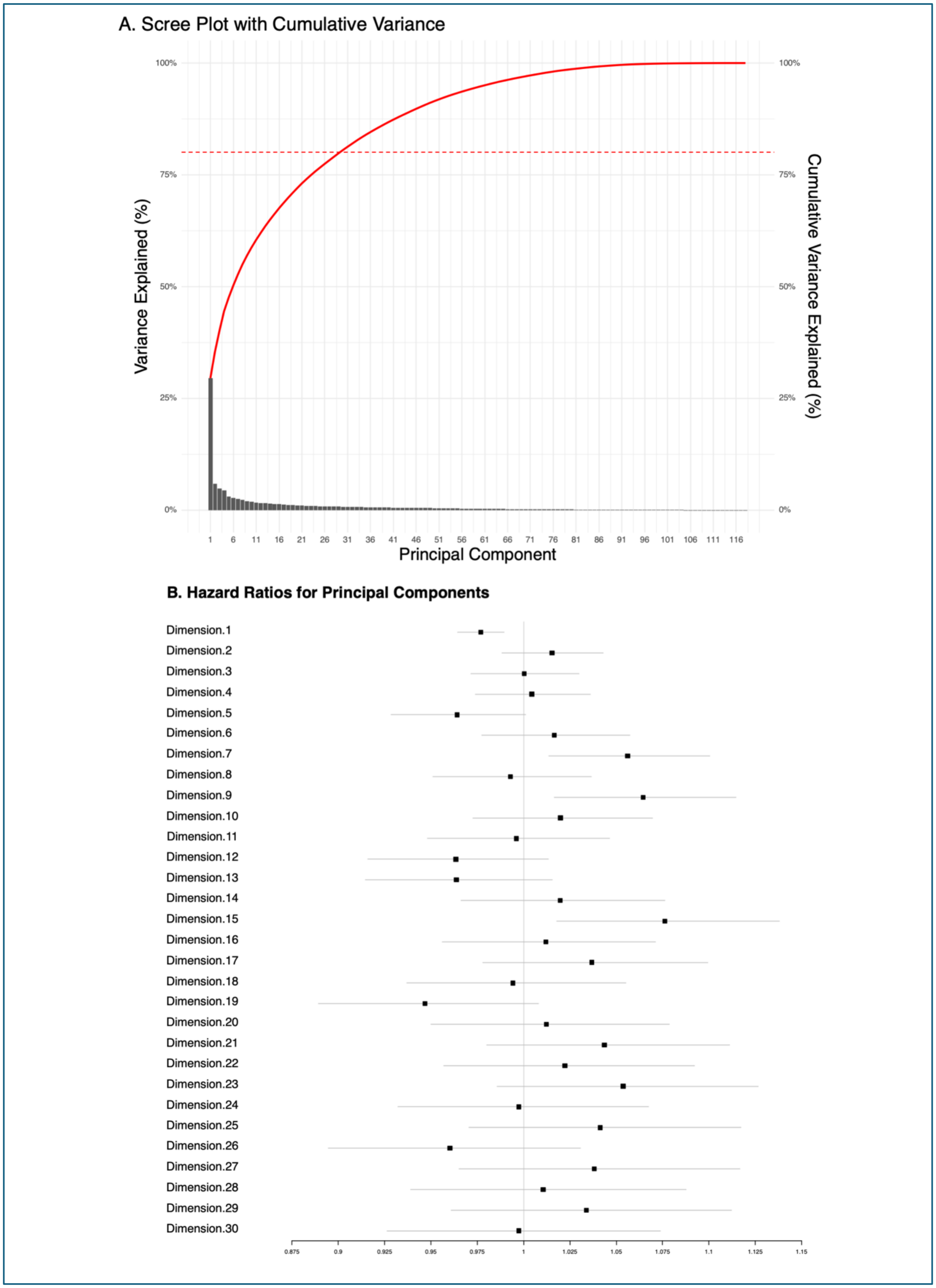
Supplementary Figure 4. Association between retinal vascular parameters and risk of incident stroke in the unadjusted model



Retinal Vascular Parameters	Unadjusted Model	HR (95% CI)	P value*
Calibre			
Central Retinal Artery Equivalent		0.786 (0.731 - 0.845)	<0.001
Length Diameter Ratio			
Arteries		1.425 (1.342 - 1.514)	<0.001
Vessels in macular region		1.262 (1.182 - 1.346)	<0.001
Complexity			
Fractal Dimension			
Arteries		0.659 (0.617 - 0.702)	<0.001
Vessels		0.693 (0.650 - 0.738)	<0.001
Number			
Arterial bifurcation points		0.639 (0.593 - 0.689)	<0.001
Arterial branching points		0.629 (0.585 - 0.677)	<0.001
Arterial nonterminal points		0.624 (0.580 - 0.671)	<0.001
Arterial segments		0.619 (0.576 - 0.665)	<0.001
Vessel segments in macular region		0.706 (0.658 - 0.757)	<0.001
Arterial terminal points		0.618 (0.574 - 0.664)	<0.001
Density			
Arc Length			
Arteries		1.444 (1.362 - 1.531)	<0.001
Vessels in macular region		1.320 (1.239 - 1.406)	<0.001
Arterial nonterminal points		1.450 (1.368 - 1.536)	<0.001
Arterial terminal points		1.364 (1.282 - 1.452)	<0.001
Bifurcation Density			
Arteries		0.707 (0.660 - 0.758)	<0.001
Branching Density			
Arteries		0.693 (0.648 - 0.740)	<0.001
Veins		0.746 (0.698 - 0.798)	<0.001
Vessels in macular region		0.773 (0.720 - 0.830)	<0.001
Chord Length			
Arteries		1.443 (1.361 - 1.530)	<0.001
Vessels in macular region		1.321 (1.240 - 1.407)	<0.001
Vesel Area Density			
Vessels		0.708 (0.662 - 0.758)	<0.001
Arteries		0.651 (0.608 - 0.698)	<0.001
Arteries in macular region		0.668 (0.624 - 0.715)	<0.001
Arteries outside macular region		0.671 (0.625 - 0.720)	<0.001
Vessel Skeleton Density			
Arteries		0.635 (0.593 - 0.681)	<0.001
Arteries in macular region		0.660 (0.618 - 0.704)	<0.001
Arteries outside macular region		0.649 (0.605 - 0.697)	<0.001
Tortuosity			
Inflection Count Tortuosity			
Arteries		0.846 (0.788 - 0.908)	<0.001

Notes: * The False Discovery Rate method was used to adjust P values at a level of 0.05. HR, hazard ratio, and CI, Confidence Interval. HR represents the relative risk of incident stroke for each 1 standard deviation increase in the exposure.

Supplementary Figure 5. Principal component analysis



Notes: A. Scree Plot with Cumulative Variance. Number of components needed to explain 80% of variance was 30. B. Hazard Ratios for Principal Components. The adjusted covariates included age, sex, systolic blood pressure, total cholesterol, HDL, HbA1c, smoking, BMI, and Indices of Multiple Deprivation.

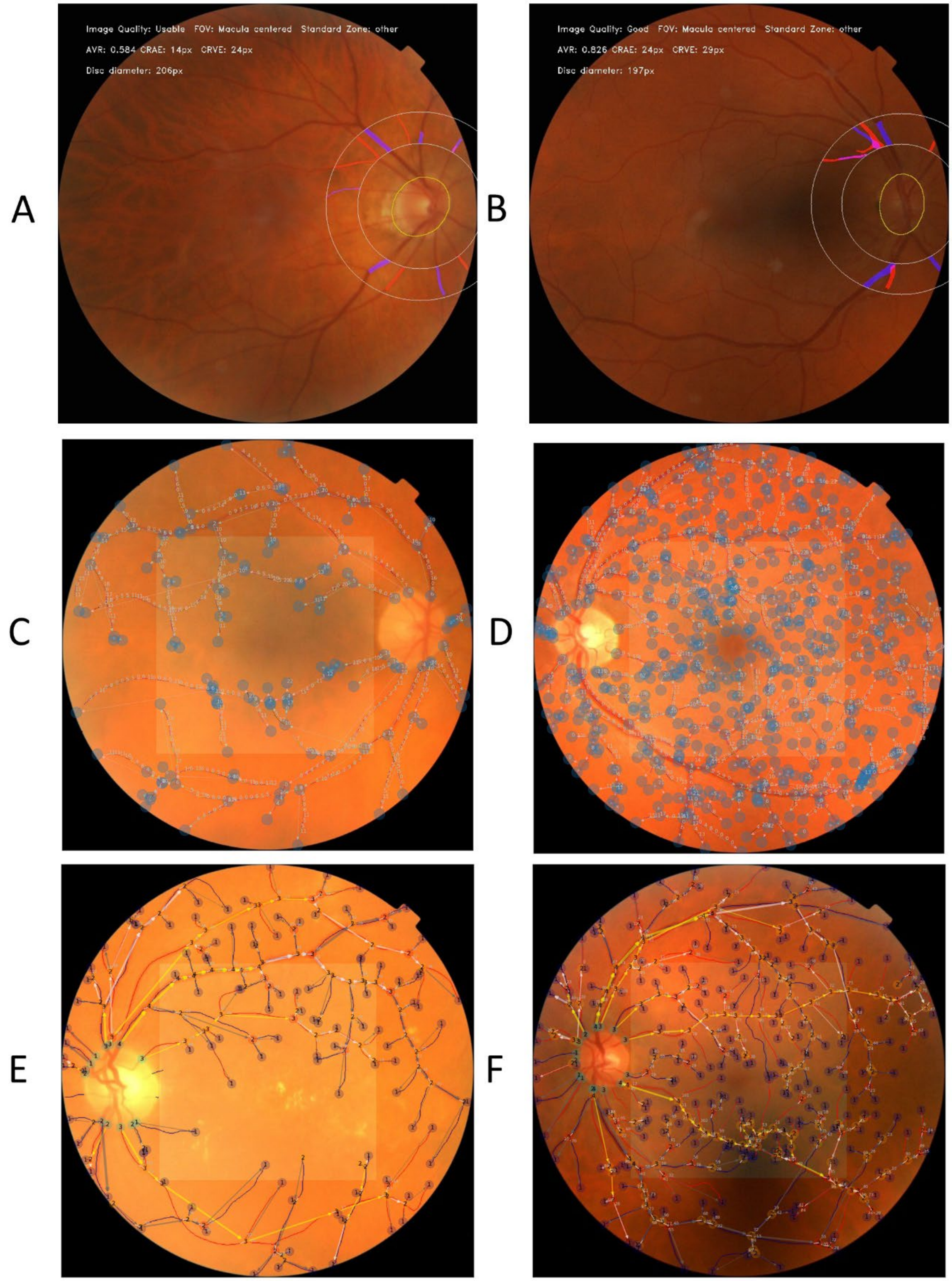
Supplementary Table 12. Values of 29 parameters in incident stroke and non-stroke subjects

	stroke free		**incident stroke**		**p value**
	N=44,412		N=749		
Variables	Median (interquartile range)	Mean (SD)	Median (interquartile range)	Mean (SD)	
Central Retinal Artery Equivalent	148.179 [137.226, 159.160]	148.552 (16.171)	145.032 [133.710, 155.002]	144.761 (16.395)	<0.001
Length Diameter Ratio (artery)	12.881 [11.941, 14.152]	13.244 (1.812)	13.601 [12.469, 15.147]	13.982 (2.080)	<0.001
Length Diameter Ratio (macula)	13.443 [12.355, 14.848]	13.784 (1.986)	13.866 [12.701, 15.522]	14.273 (2.167)	<0.001
Fractal Dimension (artery)	1.522 [1.490, 1.548]	1.516 (0.041)	1.501 [1.467, 1.532]	1.498 (0.043)	<0.001
Fractal Dimension	1.724 [1.696, 1.743]	1.717 (0.034)	1.707 [1.677, 1.733]	1.703 (0.036)	<0.001
Number of arterial bifurcation	49.000 [38.000, 60.000]	48.843 (15.491)	41.000 [31.000, 53.000]	42.493 (14.965)	<0.001
Number of arterial branching	93.000 [70.000, 114.000]	92.185 (29.578)	79.000 [56.000, 100.000]	79.322 (28.740)	<0.001
Number of nonterminal artery	85.000 [66.000, 103.000]	84.227 (25.323)	71.000 [53.000, 92.000]	72.935 (24.894)	<0.001
Number of arterial segments	165.000 [128.000, 199.000]	163.127 (47.041)	140.000 [104.000, 176.000]	141.681 (45.869)	<0.001
Number of segments in the macula	84.000 [67.000, 99.000]	82.713 (23.005)	74.000 [57.000, 93.000]	74.987 (23.993)	<0.001
Number of terminal arteries	80.000 [63.000, 96.000]	78.897 (22.138)	68.000 [51.000, 85.000]	68.749 (21.354)	<0.001
Arc length (artery)	628.581 [579.276, 699.509]	651.183 (99.836)	673.339 [608.981, 760.126]	693.133 (112.871)	<0.001
Arc length (macula)	583.215 [536.326, 643.105]	598.235 (86.319)	605.324 [553.969, 679.937]	623.444 (96.046)	<0.001
Arc length of nonterminal artery	662.528 [602.084, 750.785]	691.614 (124.608)	716.865 [632.938, 829.930]	745.372 (144.786)	<0.001
Arc length of terminal artery	590.771 [542.732, 655.010]	607.989 (90.020)	617.098 [562.661, 690.948]	637.848 (103.953)	<0.001
Bifurcation density(artery)	0.013 [0.012, 0.015]	0.013 (0.002)	0.012 [0.011, 0.014]	0.012 (0.002)	<0.001
Branching density(artery)	0.014 [0.012, 0.015]	0.014 (0.002)	0.013 [0.012, 0.014]	0.013 (0.002)	<0.001
Branching density(vein)	0.013 [0.012, 0.014]	0.013 (0.001)	0.013 [0.012, 0.014]	0.013 (0.002)	<0.001
Branching density (macula)	0.014 [0.013, 0.016]	0.014 (0.002)	0.014 [0.012, 0.015]	0.014 (0.002)	<0.001
Chord length (artery)	579.297 [533.599, 644.721]	599.894 (92.124)	619.536 [560.652, 697.897]	638.460 (104.506)	<0.001
Chord length (macula)	532.395 [490.336, 586.388]	546.052 (78.085)	551.991 [505.774, 619.078]	568.952 (87.631)	<0.001
Vessel Area Density	12.644 [11.466, 13.665]	12.506 (1.571)	12.035 [10.821, 13.112]	11.968 (1.577)	<0.001
Vessel Area Density(artery)	5.568 [4.860, 6.199]	5.504 (0.942)	5.138 [4.381, 5.813]	5.105 (0.942)	<0.001

Vessel Area Density(artery)-macula	5.123 [4.229, 5.896]	5.019 (1.209)	4.550 [3.613, 5.433]	4.525 (1.269)	<0.001
Vessel Area Density(artery)-other	5.661 [4.960, 6.315]	5.620 (0.959)	5.269 [4.583, 5.915]	5.247 (0.953)	<0.001
Vessel Skeleton Density(artery)	1.421 [1.220, 1.592]	1.399 (0.252)	1.281 [1.083, 1.477]	1.285 (0.252)	<0.001
Vessel Skeleton Density(artery)-macula	1.655 [1.363, 1.867]	1.593 (0.366)	1.459 [1.153, 1.734]	1.429 (0.390)	<0.001
Vessel Skeleton Density(artery)-other	1.357 [1.169, 1.526]	1.344 (0.243)	1.235 [1.066, 1.429]	1.243 (0.237)	<0.001
Inflection count tortuosity (artery)	0.226 [0.213, 0.238]	0.225 (0.018)	0.223 [0.210, 0.235]	0.222 (0.019)	<0.001

Notes: Kolmogorov-Smirnov was performed to test distribution normality. For comparison between groups, when both groups followed a normal distribution, a T-test was applied, otherwise, the Mann-Whitney U test was used. SD, standard deviation.

Supplementary Figure 6 representative images from stroke and stroke-free participants



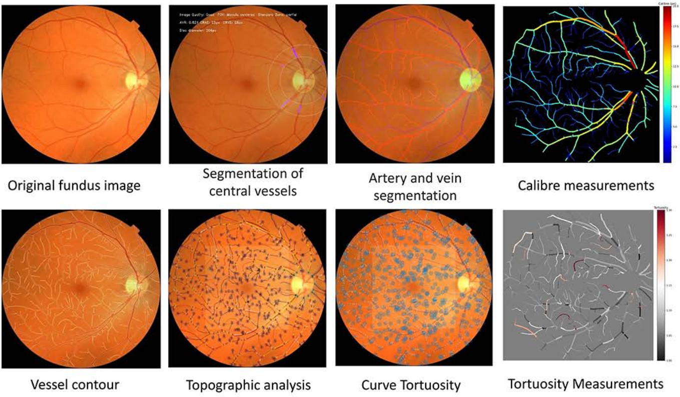
Notes. Fundus images on the left side (A, C, E) were from participants who developed incident stroke cases and images on the right side (B, D, F) were from those who remained stroke-free. Those who remained stroke-free had higher central retinal artery equivalent values, more complex, and denser vascular network in the retina.

Supplementary Text 1. Clinical implications of difference in retinal vascular parameters between stroke-free and incident stroke participants

The comparison of retinal vascular parameters between stroke-free and incident stroke participants was performed. (Supplementary Table 12) At the descriptive analysis level, Kolmogorov-Smirnov was performed to test distribution normality. For comparison between groups, when both groups followed a normal distribution, a T-test was applied, otherwise, the Mann-Whitney U test was used. The results revealed significant differences in all those parameters. Supplementary Figure 6 presents images from participants who developed stroke and remained stroke-free and provides direct visual comparisons. Especially, in Supplementary Figure 6, C vs D and E vs F show evident differences in the retinal network Complexity and Density.

In clinical practice, the presence of reduced Complexity and Density, which could be detected by the naked eye, especially by experienced eye health professionals, could serve as a warning sign for physicians to recommend lifestyle modifications, such as improved diet and increased physical activity, to enhance vascular health and consider more aggressive interventions if other risk factors are present. Some parameters, such as the central retinal artery equivalent (CRAE) and Length-to-Diameter Ratio, are not visually discernible to the naked eye. This highlights the importance of AI-assisted segmentation and quantification in identifying subtle differences that could be pivotal in stroke risk assessment. Furthermore, these findings reinforce the importance of regular retinal examinations as part of screening and prevention strategies for both ocular and systemic conditions, especially in high-risk populations.

A. Retinal vascular network analysis



Original fundus image

Segmentation of central vessels

Artery and vein segmentation

Calibre measurements

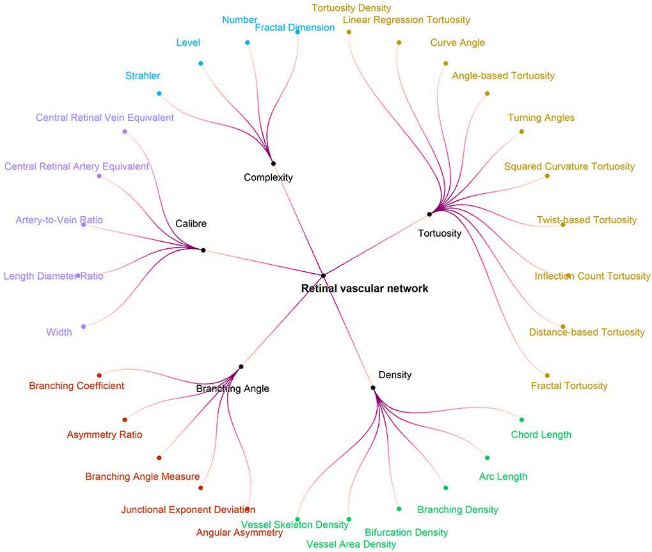
Vessel contour

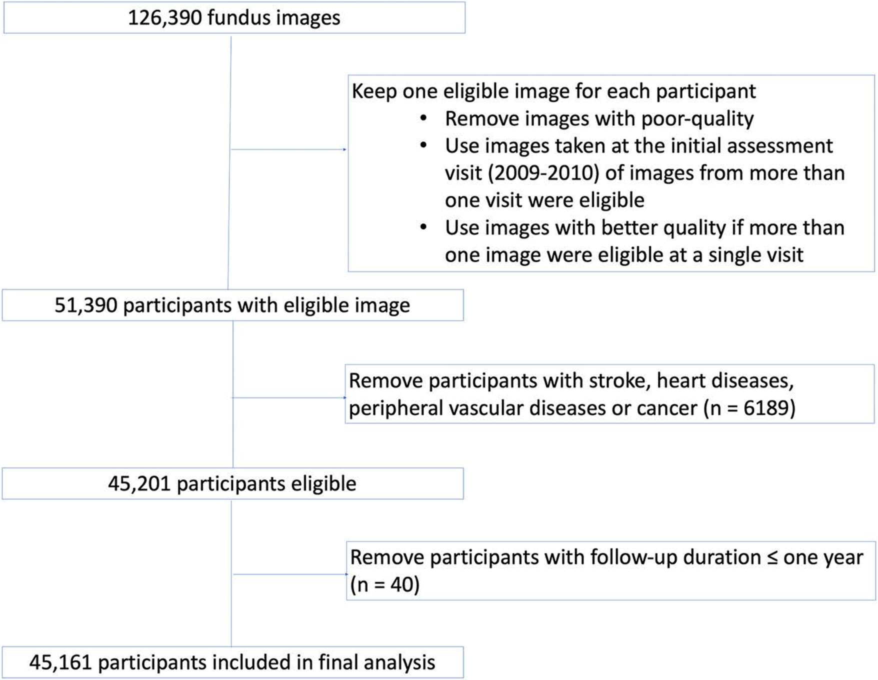
Topographic analysis

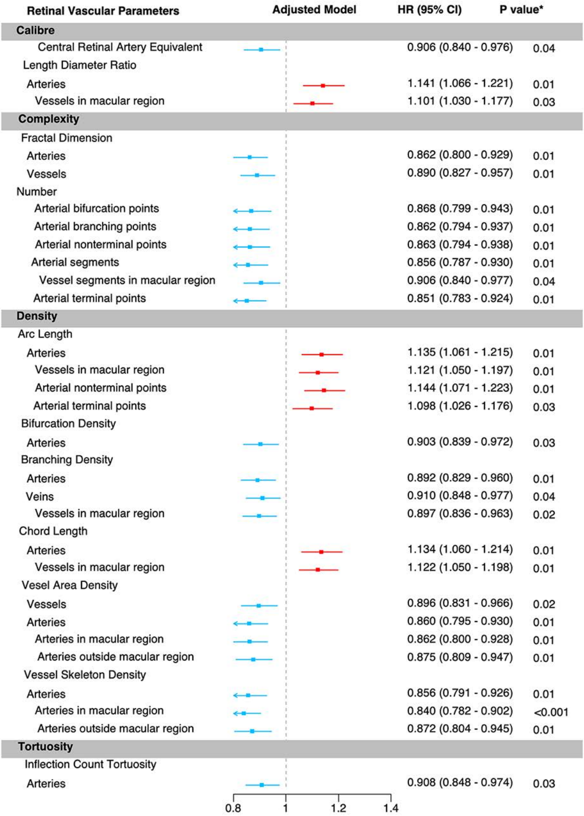
Curve Tortuosity

Tortuosity Measurements

B. Categories and Measure Types




126,390 fundus images
Keep one eligible image for each participant
• Remove images with poor-quality
• Use images taken at the initial assessment visit (2009-2010) of images from more than one visit were eligible
• Use images with better quality if more than one image were eligible at a single visit
51,390 participants with eligible image
Remove participants with stroke, heart diseases, peripheral vascular diseases or cancer (n = 6189)
45,201 participants eligible
Remove participants with follow-up duration ≤ one year (n = 40)
45,161 participants included in final analysis



Retinal Vascular Parameters	HR (95% CI)	P value*
Calibre		
Central Retinal Artery Equivalent	0.906 (0.840 - 0.976)	0.04
Length Diameter Ratio		
Arteries	1.141 (1.066 - 1.221)	0.01
Vessels in macular region	1.101 (1.030 - 1.177)	0.03
Complexity		
Fractal Dimension		
Arteries	0.862 (0.800 - 0.929)	0.01
Vessels	0.890 (0.827 - 0.957)	0.01
Number		
Arterial bifurcation points	0.868 (0.799 - 0.943)	0.01
Arterial branching points	0.862 (0.794 - 0.937)	0.01
Arterial nonterminal points	0.863 (0.794 - 0.938)	0.01
Arterial segments	0.856 (0.787 - 0.930)	0.01
Vessel segments in macular region	0.906 (0.840 - 0.977)	0.04
Arterial terminal points	0.851 (0.783 - 0.924)	0.01
Density		
Arc Length		
Arteries	1.135 (1.061 - 1.215)	0.01
Vessels in macular region	1.121 (1.050 - 1.197)	0.01
Arterial nonterminal points	1.144 (1.071 - 1.223)	0.01
Arterial terminal points	1.098 (1.026 - 1.176)	0.03
Bifurcation Density		
Arteries	0.903 (0.839 - 0.972)	0.03
Branching Density		
Arteries	0.892 (0.829 - 0.960)	0.01
Veins	0.910 (0.848 - 0.977)	0.04
Vessels in macular region	0.897 (0.836 - 0.963)	0.02
Chord Length		
Arteries	1.134 (1.060 - 1.214)	0.01
Vessels in macular region	1.122 (1.050 - 1.198)	0.01
Vesel Area Density		
Vessels	0.896 (0.831 - 0.966)	0.02
Arteries	0.860 (0.795 - 0.930)	0.01
Arteries in macular region	0.862 (0.800 - 0.928)	0.01
Arteries outside macular region	0.875 (0.809 - 0.947)	0.01
Vessel Skeleton Density		
Arteries	0.856 (0.791 - 0.926)	0.01
Arteries in macular region	0.840 (0.782 - 0.902)	<0.001
Arteries outside macular region	0.872 (0.804 - 0.945)	0.01
Tortuosity		
Inflection Count Tortuosity		
Arteries	0.908 (0.848 - 0.974)	0.03