Original research

Retinal vascular fingerprints predict incident stroke: findings from the 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 (ROC) 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 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 ROC 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.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ 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 analyse a comprehensive set of retinal vascular parameters (118 parameters in total) using fundus photographs 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 with 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 healthcare and low-resource settings.

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% of occurrences 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 hypercholesterolaemia,[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

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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.

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 laboratory 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 years across the UK 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

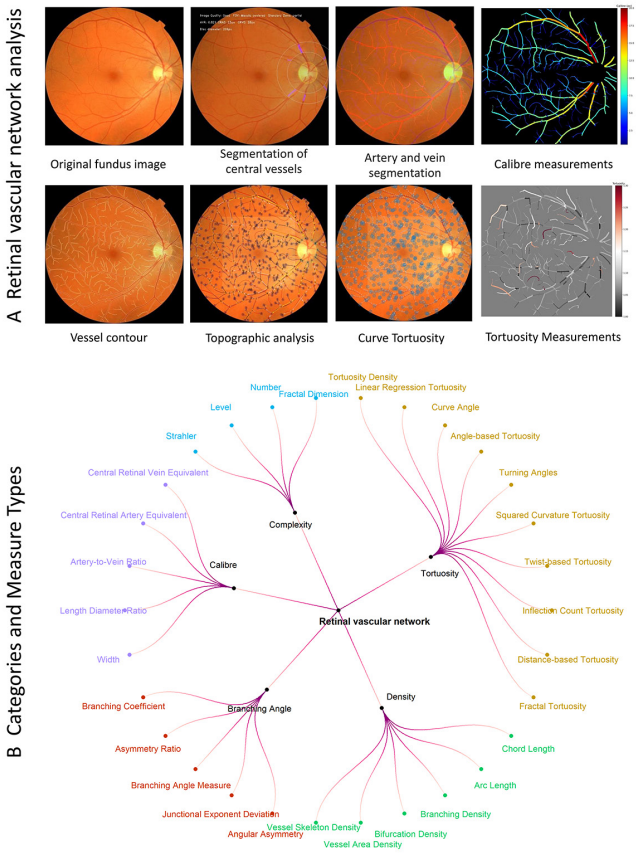

Figure 1 Retinal vascular network segmentation and quantification.

was categorised as "good", "usable" and "reject". The rejected images were considered ungradable and excluded from further analysis.[12] A total of 30 measure types of five categories – Calibre, Density, Tortuosity, Branching Angle and Complexity – were extracted. (figure 1) To minimise the potential impact of extreme values, we excluded outliers following the method proposed by Zekavat *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 haemoglobin (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 high-performance liquid chromatography analysis on a Bio-Rad VARIANT II Turbo (online supplemental table 1).

Outcome definition

We identified medical conditions using the International Classification of Diseases, Tenth Edition 10 (ICD-10) and Nineth Edition (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 (online supplemental table 1). Additionally, we excluded those who died or had a stroke attack within the first year of follow-up to minimise 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 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 nonlinear 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 3 years of follow-up; (2) including those with valid retinal images and cardiovascular risk; and (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 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, 6189 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 1 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 online supplemental 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 (IQR 12.3–12.6) years. Participants who experienced an incident stroke were significantly older (61.3±6.8 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 is noteworthy that over half (n=17) of those parameters were density parameters. Additionally, there were eight complexity parameters, three calibre parameters and one tortuosity parameter.

Calibre

Among the five calibre measure types, only central retinal artery equivalent (CRAE) and parameters of length diameter ratio (LDR) were significantly associated with the risk of incident

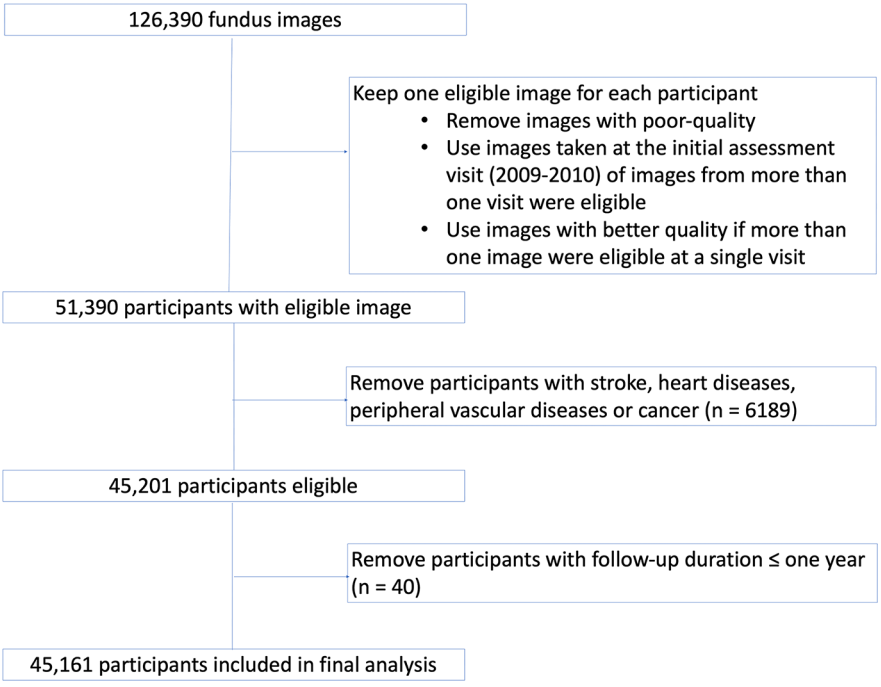

Figure 2 Study participants' selection process.

Table 1 Baseline demographic characteristics of participants

Characteristic	All (N=45 161)	Incident stroke (N=749)	Stroke-free (N=44 412)	P-value
Age (years)				<0.001
Mean (SD)	55.4 (8.18)	61.3 (6.80)	55.3 (8.17)	
Sex				<0.001
Female	24 785 (54.9%)	342 (45.7%)	24 443 (55.0%)	
Male	20 376 (45.1%)	407 (54.3%)	19 969 (45.0%)	
Ethnicity				0.39
White	41 206 (91.2%)	687 (91.7%)	40 519 (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%)	
IMD				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	17 435 (38.6%)	222 (29.6%)	17 213 (38.8%)	
Intermediate	22 388 (49.6%)	370 (49.4%)	22 018 (49.6%)	
Low	4846 (10.7%)	141 (18.8%)	4705 (10.6%)	
Missing	492 (1.1%)	16 (2.1%)	476 (1.1%)	
BMI (kg/m^2)				<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	26 250 (58.1%)	373 (49.8%)	25 877 (58.3%)	
Previous	14 642 (32.4%)	274 (36.6%)	14 368 (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	41 514 (91.9%)	685 (91.5%)	40 829 (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)	
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	43 170 (95.6%)	673 (89.9%)	42 497 (95.7%)	
Yes	1753 (3.9%)	72 (9.6%)	1681 (3.8%)	
Missing	238 (0.5%)	4 (0.5%)	234 (0.5%)	

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.
BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; IMD, Indices of Multiple Deprivation; LDL, low-density lipoprotein; SBP, systolic blood pressure; SD, standard deviation.

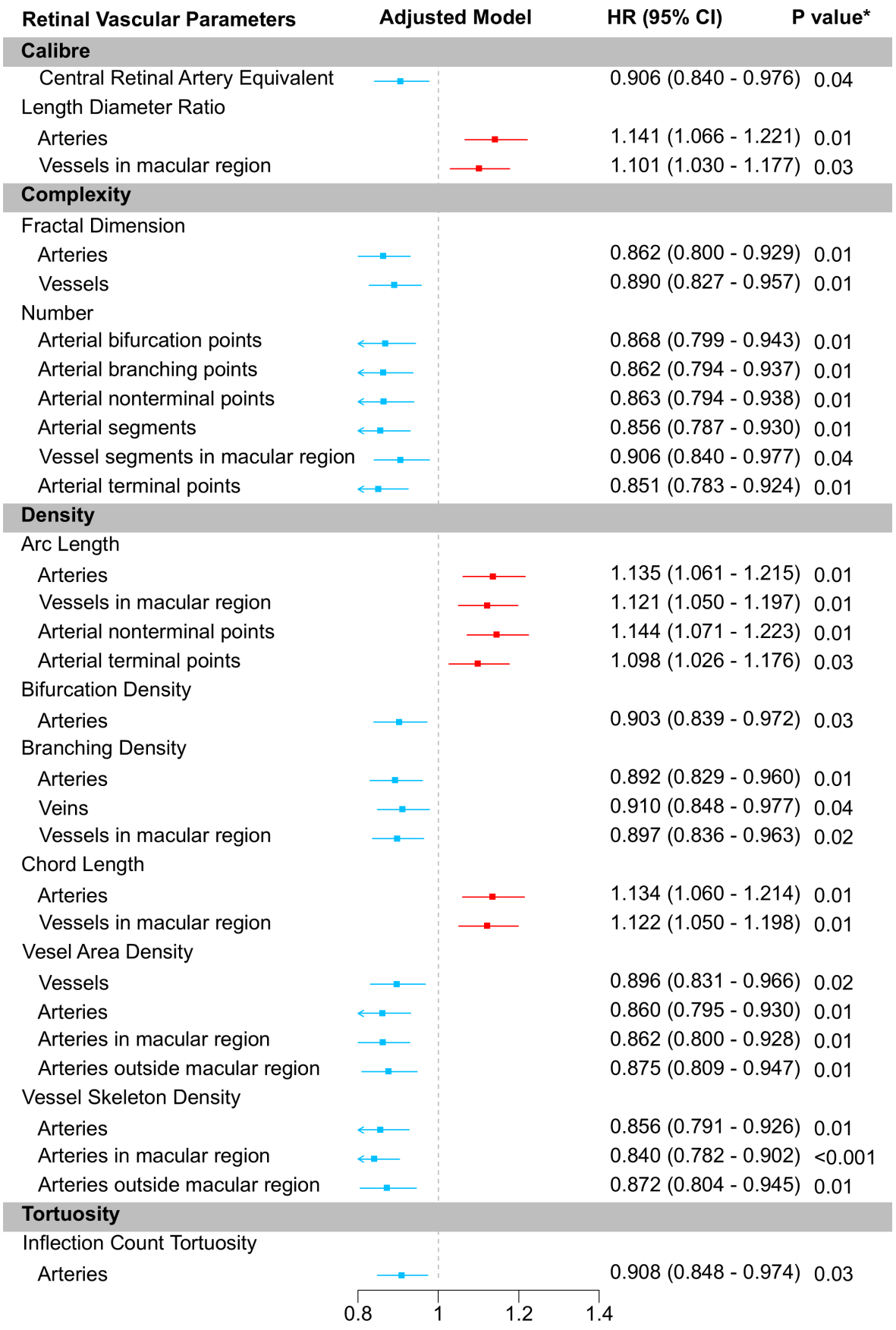

Figure 3 Association between retinal vascular parameters and risk of incident stroke. The adjusted model was adjusted for age, sex, systolic blood pressure, total cholesterol, high-density lipoprotein, glycosylated haemoglobin, smoking, body mass index and Indices of Multiple Deprivation at baseline. *The false discovery rate method was used to adjust p-values at a level of 0.05. Hazard ratio (HR) represents the relative risk of incident stroke for each standard deviation change in the exposure. The results of the unadjusted model can be found in online supplemental figure 4.

stroke in the fully adjusted model. One SD increase in CRAE was associated with a 9.4% decrease in stroke risk, with an HR of 0.906 (95% CI 0.840 to 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 to 1.221, p<0.01) and 1.101 (95% CI 1.030 to 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 1 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 1 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% to 14.4%), with HRs ranging from 1.098 to 1.144. Similarly, a 1 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 to 1.214, p<0.01) and 1.122 (95%CI 1.050 to 1.198, p<0.01), respectively.

Notably, decreases in other identified density parameters were all associated with increased stroke risk. Specifically, 1 SD decrease in arterial bifurcation density increased risk by 10.7%, and 1 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 (online supplemental 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.

Nonlinear association, subgroup and sensitivity analyses

Among 29 identified parameters, only number of vessel segments in the macular region showed a nonlinear association, an L-pattern with HR decreasing with increase in the number and then levelling off when the number reached 60 (online supplemental 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 nonlinear associations (online supplemental figure 2 and table 4). Furthermore, the sensitivity analyses showed 27 of 29 remained significant associations when individuals with cardiovascular disease risk were kept and all maintained significance in the other two analyses (online supplemental figure 3). Exploration of principal component analysis can be found in online supplemental figure 5. Online supplemental tables 5–10 show the results of subgroup analyses. Please refer to online supplemental table 11 for the full list of retinal vascular parameters.

DISCUSSION

This study represents a comprehensive exploration of retinal vascular parameters, encompassing 118 measurements across 30 distinct measure types categorised 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 that 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 emphasises 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 photographs. 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 healthcare and low-resource settings. In addition, a previous study demonstrated the cost-effectiveness of retinal fundus-based artificial intelligence (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. For detailed clinical implications of this study, please refer to online supplemental figure 6, supplemental table 12 and supplemental text.

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 the FDR method. It is 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 randomised 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 generalisability of the findings is limited. We also recognise 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-coded data collected during hospitalisation to identify incident strokes. This may underestimate stroke incidence since patients with mild stroke are not necessarily hospitalised. 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, eight complexity, three calibre and one tortuosifigurey 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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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and ethical approval for the UK Biobank study was obtained from the North-West Multi-Centre Research Ethics Committee (06/MRE08/65). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. This study used data from a public, open-access repository, the UK Biobank study (https://www.ukbiobank.ac.uk/).

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