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Cardiovascular Disease Classification through Retinal Fundus Image Analysis and Clinical Feature Integration

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***Abstract*— Cardiovascular illnesses remain a primary cause of morbidity and mortality in the world, highlighting the need for early, reliable, and non-invasive risk assessment tools. The retinal fundus imaging could be a useful tool for cardiovascular screening as it reflects the microvascular and haemodynamic changes associated with cardiovascular diseases. However, the extent to which retinal image-derived features can be used to predict cardiovascular risk is unknown.**

We present a machine learning-based approach to estimate cardiovascular risk based on retinal fundus images in this article. 230 fundus pictures were analysed, 115 cardiac and 115 non-cardiac individuals. Following image pre-processing, retinal features were extracted and used for training using machine learning classifiers. The independent test set and standard classification measures were used to assess model performance.

The Random Forest model has achieved the highest accuracy of 84.78% among all the tested models. The results indicate that ensemble learning can be particularly effective for detecting non-linear retinal patterns associated with cardiovascular risk.

Results in this study demonstrated that the retinal fundus image contains valuable information for cardiovascular risk assessment and can be a good starting point for future multi-modal assessment frameworks based on retinal imaging, combined with clinical biomarkers. This method serves as an example of the potential of retinal imaging as an early cardiovascular risk assessment tool that is non-invasive and scalable.

***Keywords*— Cardiovascular disease, Retinal Fundus imaging, Hybrid risk assessment, Computer vision and Feature Engineering.**

I. INTRODUCTION

Cardiovascular diseases (CVDs) remain one of the most serious global health issues, accounting for a major part of premature death and long-term disability globally [1]. Despite breakthroughs in diagnostic technologies and treatment measures, a considerable percentage of cardiovascular events occur unexpectedly, sometimes in people who have no obvious clinical symptoms. This emphasises the important need for early, accessible, and non-invasive technologies capable of detecting cardiovascular risk at the subclinical stage [2].

Clinical indicators such as age, blood pressure, lipid profiles, glycaemic markers, and lifestyle factors such as smoking and alcohol intake play a significant role in conventional cardiovascular risk assessment [3].

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While these indications have therapeutic value, they frequently fail to detect early microvascular changes that occur before apparent systemic dysfunction. Furthermore, routine cardiovascular screening techniques might be intrusive, expensive, or unfeasible for large-scale population screening, especially in resource-constrained countries [4].

In recent years, retinal fundus imaging has received increased attention as a possible surrogate sign for systemic cardiovascular function. The retina provides a unique view of the body's microcirculation, allowing direct visualisation of blood vessels without the need for intrusive operations. Variations in artery calibre, tortuosity, branching patterns, and microvascular density in the retinal vasculature have been linked to hypertension, diabetes, atherosclerosis, and other cardiovascular diseases [5-7]. These findings highlight retinal imaging as a promising technique for assessing cardiovascular risk. Figure 1 shows the structural and functional changes in the retinal vasculature, including arteriolar narrowing and vascular remodelling, reflect systemic cardiovascular risk and can be non-invasively assessed using fundus imaging.

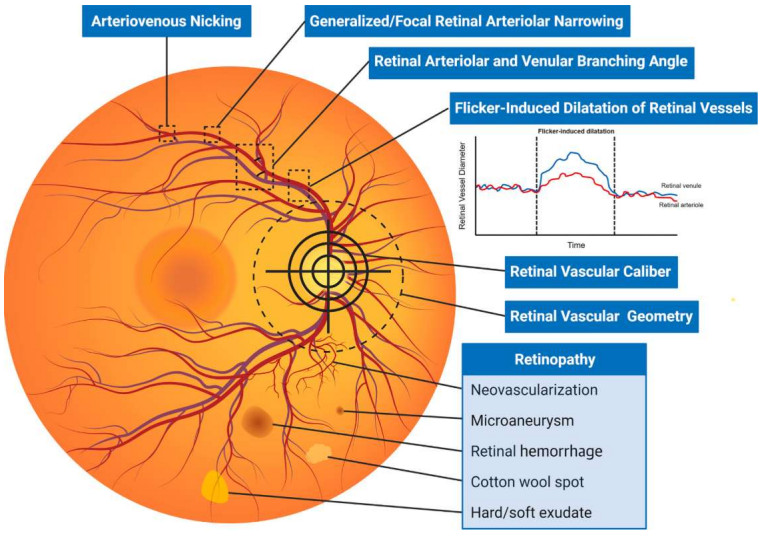

Figure 1. A schematic overview of retinal microvasculature biomarkers relevant to cardiovascular risk assessment [14]

With the rapid improvement of machine learning techniques, computational analysis of retinal fundus pictures has allowed for the extraction of subtle and complicated properties that are frequently undetected to human viewers. Several studies have established the potential of utilising retinal pictures to predict cardiovascular outcomes such as coronary artery disease, stroke risk, and severe adverse cardiac events [8–10]. However, many existing techniques rely on a small number of handcrafted features or are primarily concerned with vessel segmentation, which may fail to capture the holistic retinal signals associated with cardiovascular risk.

Furthermore, a major weakness in existing work is the inclination to analyse retinal imaging data and clinical indicators separately. Considering that cardiovascular disease is a complex disease, it is possible that models using a single data stream will not capture the full picture of patient risk. Retinal image-derived features can be combined with routinely acquired clinical parameters like blood pressure, heart rate, glycaemic state, and lifestyle factors which can enhance prediction accuracy and increase the clinical interpretability [11-13]. However, study of the independent utility of the retinal image features as a basis for these multi-modal frameworks is still limited.

Motivated by these shortcomings, the current study looks into the efficiency of retinal fundus image-based machine learning models for binary cardiovascular risk prediction. The aim of the present study is to develop a robust baseline for retinal image-based cardiovascular risk assessment using multiple classification algorithms and obtaining a high-dimensional feature representation from the fundus images. The study results will be used to develop new multi-modal risk prediction systems based on retinal imaging and clinical blood markers to enable readily scalable, non-invasive cardiovascular screening in real-world clinical settings.

Retinal fundus photography offers a signal from the image that reflects the microvascular health of the system from a biomedical engineering standpoint. The fact that these images are being captured routinely in many ophthalmology clinics means that they could provide a non-invasive, complementary method to current screening without burdening patients or health systems with extra burden when assessing for cardiovascular risk.

II. RELATED WORK

Historically, cardiovascular risk prediction has relied on clinical and epidemiological studies in which a variety of demographic, physiological and lifestyle factors have been used to predict future cardiovascular outcomes. Although they have been important to either preventive cardiology or clinical decision-making, these models are predominantly based on systemic markers that are often associated with the presence of disease rather than its early onset [15]. Consequently, the emphasis has gradually shifted to developing alternative indicators that would be able to detect cardiovascular risk much earlier.

In this context, the retinal vasculature has received a lot of study due to its tight physiological interaction with systemic microcirculation. The vessels can be directly observed in vivo in the retina, which means that the microvascular anatomy of the retina can be evaluated without causing any pain or discomfort. In earlier population-based studies, there was a consistent association between the constriction of the retinal arterioles, nicking of arterioles and the development of cardiovascular outcomes associated with hypertension [16,17]. In longitudinal studies alterations in retinal vascular calibre were linked with coronary heart disease and cardiovascular mortality, thus reinforcing the theory that retinal microvascular changes were associated to larger cardiovascular pathology [18].

With increased availability of digital fundus images, computational tools were introduced to the traditional clinical evaluation. Initial studies were conducted focusing mainly on the artificial retinal characteristics including the diameter, tortuosity and branching geometry of the vessels, which were demonstrated to be linked with cardiovascular risk factors like diabetes, hypertension and smoking [19]. All these methods were successful in shedding light on these questions, but they were also not very robust and not easily applied to the wide variety of images encountered in clinical practice, as they depended on accurate segmentation of the vessel and were sensitive to image quality.

Recently, the use of machine learning and deep learning methods has been investigated to tackle this limitation by learning complex patterns directly from retinal images. In several studies, it has been demonstrated that information can be extracted from the pictures of the retina that seems to be able to predict cardiovascular risk factors like age, blood pressure and smoking [20]. The results from these conclusions show that retinal photographs contain information regarding retinal health and known vascular measures of systemic health. The below approaches were further advanced to predict cardiovascular disease, stroke risk and mortality in convolutional neural networks and ensemble based models [21, 22]. All of them are promising approaches, but some are black-box approaches and are not necessarily interpretable and do not necessarily inspire therapeutic trust.

TABLE I. SUMMARY OF EXISTING STUDIES ON RETINAL IMAGING BASED CARDIOVASCULAR RISK ANALYSIS

Ref	Data Modality	Methodology Used	Results (Key Findings)	Limitations / Gaps
[08]	Retinal fundus images	Deep learning models	Predicted cardiovascular risk factors directly from retinal images	Limited interpretability
[10]	Retinal images	Computational image analysis	Demonstrated feasibility of automated retinal analysis	Sensitive to image quality
[15]	Clinical data	Population-based risk modeling	Established age, BP, and lifestyle factors as predictors of CVD risk	Does not capture microvascular-level changes
[16]	Retinal fundus images	Manual retinal vessel analysis	Found retinal arteriolar narrowing associated with hypertension-related CVD	Focused on limited retinal signs
[17]	Retinal microvascular data	Epidemiological analysis	Reported association between retinal abnormalities and CVD mortality	Observational, not predictive
[18]	Retinal vascular caliber	Statistical correlation analysis	Demonstrated link between vessel caliber and coronary heart disease risk	Single retinal metric analyzed
[19]	Retinal images	Handcrafted feature extraction	Showed retinal structural features correlate with CVD risk factors	Dependent on vessel segmentation
[22]	Clinical records (EHR)	Machine learning on structured data	Clinical variables effectively used for disease risk prediction	Imaging information not considered
[21]	Retinal images	CNN-based prediction	Achieved promising CVD and stroke risk prediction	Requires large datasets
[22]	Retinal + clinical data	Multi-modal feature fusion	Improved prediction using combined retinal and clinical features	Contribution of each modality unclear
[23]	Retinal + clinical data	Integrated learning models	Enhanced systemic disease risk estimation	Limited standalone retinal evaluation

The merging of retinal imaging with structured clinical information is another emerging theme of the literature. Due to its complex nature, cardiovascular diseases have been shown to achieve better prediction effectiveness by

combining retinal disease markers with the usual clinical markers [23] and [24]. In many instances, however, the fusion procedures take precedence to the demonstration of the ability of the retinal image-derived features to discriminate independently, which makes it difficult to study the contribution of each modality.

In general, a comprehensive literature review indicates that studies on retinal imaging as a tool for CV risk prediction are at their infancy. Although several studies have pointed towards the potential of retinal fundus pictures as non-invasive biomarkers, the number of studies that focus on systematical evaluation, using typical machine learning classifiers, is still limited. Moreover, there are few studies based in hospitals with moderate sample sizes, which, again, is due to practical limitations in data collection for well-annotated retinal and cardiovascular data. The above constraints highlight areas for further research in this area, such as the creation of strong baselines and therapeutically viable models for the future use of multi-modal cardiovascular risk assessment frameworks. Table 1 shows a comparison of existing studies on retinal imaging and predicting cardiovascular risk. It demonstrates that the methodologies are different and what further research is needed to fill the gaps.

From the Table 1 it is observed that previous studies have shown that retinal imaging could be useful for assessing cardiovascular risk. However, the fact that there are many different methods and not many systematic evaluations shows that this field of research is still growing.

III. MATERIAL AND METHOD USED

A. Study setting and Data resource

This study was conducted utilising retrospective data gathered at JSS Hospital, Mysuru by the Departments of Cardiology and Ophthalmology in partnership. Patients who had routine retinal fundus imaging and cardiovascular examination were examined for inclusion. Only cases with complete retinal scans and clinical information were considered for the investigation.

The study included 230 participants, with 115 being cardiac and 115 non-cardiac. Each subject's heart status was assessed using clinical diagnoses from cardiology reports. The balanced distribution of classes was deliberately maintained to avoid bias during model training and evaluation. The overall methodology is illustrated in figure 2.

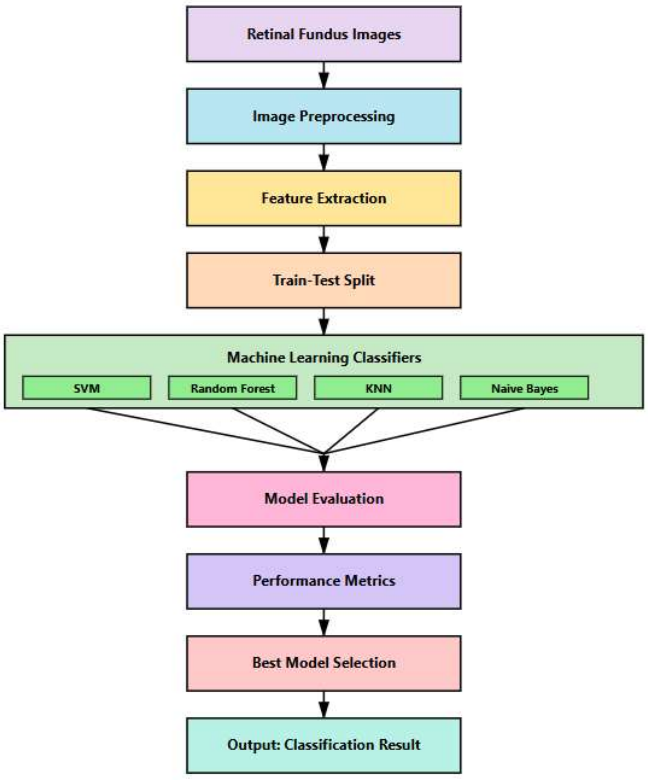

Figure 2. Block diagram of suggested methodology

B. Clinical data acquisition and representation

Hospital records were used to acquire regularly collected clinical parameters in addition to retinal imaging. Age, gender, blood pressure, heart rate, glycaemic status, HbA1c, diabetes, body weight, smoking, and alcohol use were among them. In order to ensure temporal alignment between imaging and physiological data, these variables, which are frequently utilised in cardiovascular risk assessment, were acquired during the same clinical visit as retinal image acquisition.

A systematic comma-separated values (CSV) format was used to organise clinical data. While continuous variables were normalised before analysis to lessen the impact of scale disparities during model learning, categorical variables like gender, smoking status, alcohol intake, and diabetes status were numerically encoded. The main focus of the current research was on features extracted from retinal images, even if clinical features were prepared for integration.

C. Retinal fundus image dataset

When collecting retinal fundus images, the ophthalmology department followed normal clinical fundus photography procedures. Images from both cardiac and non-cardiac individuals were organised into distinct files. Only images with an appropriate field of view, illumination, and focus were chosen for further processing. Images containing motion blur, low contrast, or acquisition artefacts were removed during the manual examination.

D. Feature extraction

Handcrafted retinal features and clinical features were extracted to characterize retinal abnormalities associated with cardiovascular disease.

Handcrafted features

In the first step, hand-made retinal biomarkers were derived from the pre-processed fundus images. The extracted features were texture descriptors, statistical intensity measures, transform domain features, and retinal vascular calibre features.

Gray-Level Co-occurrence Matrix (GLCM)-based textural features such as contrast, correlation, homogeneity, energy and entropy were computed. The mean, variance, skewness and standard deviation of the retinal pixels were obtained as statistical intensities to describe the distribution of these pixels in retinal regions.

The frequency domain information was captured using the transform domain features extracted using wavelet-based representation. Retinal vascular calibre measurements were also calculated to assess the thickness of the vessels and microvascular changes linked to cardiovascular changes.

These handcrafted retinal features were then used in conjunction with clinically-relevant parameters to assemble a full set of cardiovascular feature representation.

Feature Normalization

All the extracted features were standardized using z-score normalization to ensure that features having different scales would contribute equally to the classification models. This phase allowed no features with larger numerical ranges to take over the learning process.

E. Data partitioning

There were 230 samples, equivalent to 230 retinal fundus images, and 115 cardiac patients and 115 non-cardiac patients were equally distributed. All samples were individual persons and consisted of a photograph of the retina and patient information.

To construct and evaluate models, the dataset was separated into training and testing subsets using an 80:20 hold-out technique. As a result, 230 samples were allotted for training, including 92 cardiac and 92 non-cardiac cases, with the remaining 46 samples (23 cardiac and 23 non-cardiac) saved for independent testing.

Class balance was maintained in both subsets to ensure that differential class representation did not influence cross-model performance comparisons.

F. Classification Model

Four different machine learning classifiers were used and tested to determine the most successful approach for cardiac vs. non-cardiac classification:

Support Vector Machine

A Support Vector Machine (SVM) with Radial Basis Function (RBF) kernel was developed with the following hyperparameters:

- kernel function: RBF (for non-linear classification).
- Box restriction is 1.0.
- Kernel scale: automatically optimised.
- Feature standardisation is enabled.

The SVM was chosen because of its effectiveness in high-dimensional feature spaces and capacity to discover the best separation hyperplanes for classes.

Random Forest

An ensemble classifier of 100 decision trees was developed with the following configuration:

- Total number of trees: 100.
- Minimum leaf size: 5
- Out-of-bag (OOB) prediction: enabled.
- Feature importance calculation: enabled.

Random Forest was chosen because of its resistance to overfitting, capacity to handle high-dimensional data, and supply of feature importance measures.

K-Nearest Neighbors (KNN)

A KNN classifier was implemented with the following specifications:

- Number of neighbours (k): 5.
- Distance metric: Euclidean.
- Feature standardisation: enabled.

KNN acted as a non-parametric baseline classifier, making predictions based on local.

Naive Bayes

As a probabilistic baseline model, we used a Gaussian Naive Bayes classifier. Despite its simple independence assumption, Naive Bayes frequently performs well in practice and provides probability estimates for predictions.

G. Model Evaluation

A standalone test set was used to examine model performance, which was then evaluated using standard classification measures such as accuracy, sensitivity, specificity, and F1 score. Confusion matrices were created to evaluate categorisation results in terms of true positives, true negatives, false positives, and false negatives.
The SVM classifier was also subjected to receiver operating characteristic (ROC) analysis, with the area under the curve (AUC) generated to assess discrimination performance across decision thresholds.

Confusion Matrix Analysis

Confusion matrices were created for all four models, displaying:

- True Negatives (TN): Non-cardiac patients accurately classified
- False Positives (FP): Non-cardiac patients misdiagnosed as cardiac
- False Negative (FN): Cardiac patients were misclassified as non-cardiac.
- True positives (TP): Cardiac patients were appropriately classified

Row and column normalisation were used to make it easier to interpret class-specific performance.

IV. Results and Discussion

An independent test set of 230 retinal fundus images was used for evaluating the performance of the proposed framework. There were 46 samples equally distributed between cardiac and non-cardiac patients in the test set. Four classifiers based on machine learning were used for training and testing the retinal image derived characteristics and then compared for their ability to distinguish between the two groups.
The model that performed the most consistently and reliably across all models tested was the Random Forest classifier. It has a balanced sensitivity and specificity and an accuracy of 84.78%. This balance suggests that the model was successful not only at detecting cardiac instances, but also at correctly identifying non-cardiac instances, particularly vital in screening-oriented applications where missed detections and false alarms may have clinical implications.
The Support Vector Machine gave the same results with 80.43% accuracy. Its sensitivity was slightly greater than its specificity, indicating a bias towards detecting cardiac patients. In a clinical context, this practice could be acceptable in the context of screening activities where the identification of potential high-risk people is often the highest priority even though it may result in additional follow-up evaluations.

The k-Nearest Neighbors classifier, on the other hand, had a significantly poorer performance. While this is not surprising, because distance methods have been found to perform poorly in high-dimensional feature spaces, particularly in spaces where the features represent complex interrelated patterns, as is true for the retinal image representations. The Naïve Bayes classifier had moderate accuracy, possibly due to assuming feature independence, an assumption that is unlikely to be true in the case of the features extracted from deep representations of the retina.

Table 2 shows a summary of the quantitative performance achieved with various classifiers. Comparative results further support the notion that ensemble-based methods are more appropriate for the non-linear and distributed nature of the retinal patterns as related to cardiovascular condition.

TABLE II. PERFORMANCE COMPARISON OF CLASSIFICATION MODELS USING RETINAL FUNDUS IMAGE FEATURES

Model	Accuracy (%)	Sensitivity (%)	Specificity (%)	F1-score (%)
Support Vector Machine (SVM)	80.43	82.61	78.26	80.85
Random Forest (RF)	84.78	86.96	82.61	85.11
k-Nearest Neighbors (KNN)	63.04	60.87	65.22	62.22
Naive Bayes (NB)	71.74	65.22	78.26	69.77

In addition to the quantitative results, these findings provide insights on the significance of retinal imaging in cardiovascular risk assessment. Consistent classification ability of retinal characteristics indicates that cardiovascular illness is associated with subtle image-wide changes in the retina, not with obvious local changes or abnormalities. This demonstrates the importance of retinal fundus imaging for cardiovascular risk assessment, which is a non-invasive and scalable procedure. The confusion matrix for the best performing model using the Random Forest classifier is shown in Figure 3, and is a further illustration of the classification behaviour of the best performing model.

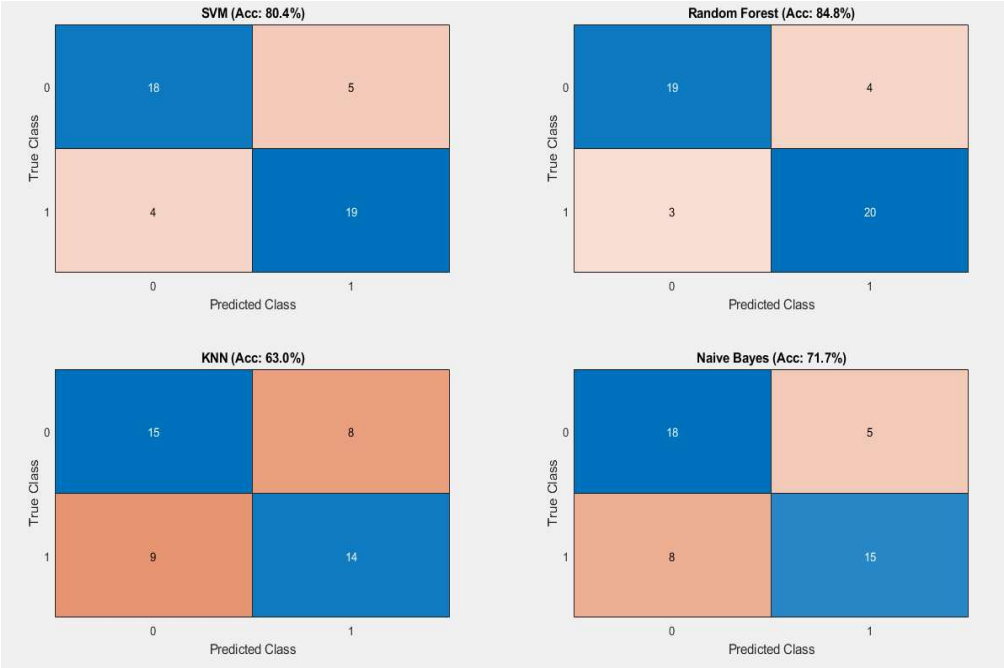

Figure 3. Confusion matrices for all models

The discriminative capability of the classifier across different decision thresholds was further examined using receiver operating characteristic analysis, as shown in Figure 4.

Meanwhile, the results show that the selection of a model is crucial when using high-dimensional retinal features. Although simpler classifiers can be interpretable, more flexible learning strategies seem to be required to fully make use of the information contained in retinal images. Importantly, the performance that was measured in this study was with data obtained in a hospital setting and a moderate sample size, so it was in real clinical environments rather than ideal experimental environments.

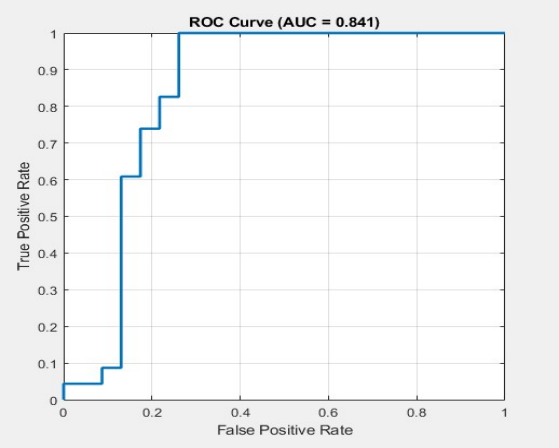

Figure 4. Receiver operating characteristic (ROC) curve for the classification model

To understand how much each feature is contributing to the classification process, feature importance scores from the Random Forest model are shown in Figure 5.

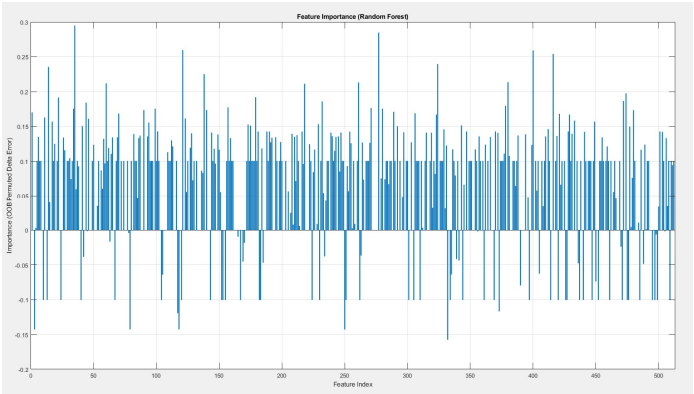

Figure 5. Feature importance scores obtained from the Random Forest classifier.

V. Conclusion and Future Direction

In this study we evaluated if retinal fundus images obtained during everyday ophthalmological examination contain meaningful data to discriminate cardiac from non-cardiac subjects. The study shows that, even if taken alone, the image-derived features can provide meaningful information about the cardiovascular status, as assessed by the performance of the different classification models applied to the hospital-based data.

One of the interesting things about this study is that the retinal patterns that are linked to cardiovascular risk don't seem to be restricted to a specific anatomical structure or a specific area. Instead they appear to arise from many minute and patchy changes in the retinal image. This is in line with previous studies showing strong association between retinal microvascular changes and systemic cardiovascular disease [16] [18]. Ensemble-based methods showed more consistent performance in the present experiments, which may be due to these distributed patterns.

The trials were conducted in actual clinical settings with a moderate-sized data set that was gathered via hospital routines, not in controlled research imaging settings. Therefore, it is important to note that the results are meant to be considered as a guide to practical feasibility and not to maximal predictive performance. This is good news from a clinical viewpoint because it indicates that the imaging of the retina might be useful in the cardiovascular risk evaluation without requiring extra invasive or resource-consuming procedures.

Meanwhile, there are a number of restrictions to consider. In the current analysis, emphasis was placed on retinal image based features and as such these forms a baseline assessment and are not a complete assessment for cardiovascular risk. Cardiovascular disease is by its nature multifactorial and using only one modality could not

comprehensively identify patient risk. Also, findings may not be easily generalizable to other clinical centers that have used data from the same center.

This finding could be explored in a number of ways in future research. The routine collection of clinical variables including blood pressure, glycemic markers, and lifestyle variables may be useful to better capture cardiovascular risk along with retinal features [22, 23]. The inclusion of multi-center cohorts and follow-up data over time may further help to elucidate the relationship between retinal changes and disease progression over time. Furthermore, leveraging approaches to enhance transparency and interpretability might be a way to help close the loop between the computations and clinical decision making.

Overall, this work contributes to the growing albeit limited evidence that using retinal fundus imagery as a non-invasive window into systemic cardiovascular function is possible. As research on this topic is still in its infancy, further studies using clinically relevant information and modelling techniques are likely to improve understanding of the role of retinal imaging for cardiovascular risk assessment.

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