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Retinal Imaging and Machine Learning: A Comprehensive Review on Cardio vascular Disease Prediction

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***Abstract*— Around 33% of deaths are occurring only because of cardiovascular diseases globally indicating that CVDs are one among the leading cause of mortality and morbidity worldwide. This results in huge economic challenges and also burdens healthcare systems. As CVDs turns out to be a major health challenge, it is highly essential to detect the symptoms of these diseases as early as possible through which early preventive therapeutic interventions are made possible thereby attenuating the impact of the disease. Most of the conventional methods used in diagnosing these diseases demands exhaustive clinical testing and it may require invasive method of investigation as well. Also, these methods may turn out to be expensive and inaccessible for a major portion of people in developing country like India. Hence the need arises to come out with non-invasive, cost- effective and innovative approach to predict CVDs. One such promising approach is to make use of retinal imaging as an excellent source of CVD risk biomarkers which provides us a way to understand the anatomical structure of the heart and hence helps in early detection of CVDs.**

The microvascular structure of the retina epitomizes the overall health status of the cardiovascular system. The fine- drawn modifications in the retinal blood vessels such as alteration in vessel diameter, tortuosity, and the presence of microaneurysms are associated with cardiovascular diseases like hypertension, coronary artery disease, and stroke.

The advent of Machine Learning techniques has greatly improved the potential of using retinal imaging to predict cardiovascular diseases by efficiently analyzing complex data to uncover the patterns that traditional methods might miss. Thereby provides an efficient, cost-effective, non-invasive, and scalable solution for automated prediction of CVDs.

This paper focuses on understanding the Machine Learning techniques, datasets and performance evaluation metrics that are used in prediction of cardiovascular diseases in most of our previous research papers and identifying the research gaps, challenges that our researchers faced during their research. To come up with open challenges and to make use of these knowledge in building a new model which is more stable accurate that can be integrated in clinical practice.

***Index Terms*— Cardiovascular Diseases–CVDs, Atherosclerotic Cardiovascular Disease – ASCVD.**

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I. INTRODUCTION

The Cardiovascular diseases (CVDs) stand as one among the prominent cause of deaths globally and hence is considered as a significant global health challenge [1]. This emphasizes the need of having an early prediction of CVDs to alleviate associated risks [4]. Retinal imaging is a major ray of hope in this regard which promises non-invasive approach for assessing cardiovascular risks [3] [4] for a rea-son that abnormalities in the microvascular structure of retina is a clear indication of broader vascu-lar health [9] [27]. Anomalies such as tortuosity, dilation and constriction present within retinal mi-crovasculature are directly associated with high risk of developing CVDs [2][6][11]. Anatomical structure of retina and heart as well as kidneys are similar [5]. As a result, extraction of features from retinal images such as retinal vessel segmentation becomes very essential in analysing the structural and pathological condition of blood vessels within the retina and in turn heart. Such analyses not only facilitate the identification of systemic health issues but also provide valuable information re-garding ocular diseases [16].

Atherosclerotic cardiovascular disease (ASCVD) remains as a leading cause of death worldwide. Identifying individuals at high risk is very much essential for preventive measures. Retinal imaging provides an alternative way for assessing ASCVD risk, especially in diabetic populations which re-places invasive methods used in traditional clinical evaluations [3]. Retinal images are analysed us-ing Deep learning methods, especially convolutional neural networks (CNNs) to come up with pre-dictive biomarkers associated with cardiovascular risk factors [4]. Retinal arteriolar narrowing (CRAE) was remarkably connected with incident MI in both age-gender-adjusted models and multi-variable model CRF significantly predicts the incident MI [7].

II. MACHINE LEARNING IN RETINAL IMAGE ANALYSIS

Predicting cardiovascular diseases (CVDs) using retinal images can be significantly improved by using machine learning algorithms. Numerous studies have explored this approach, taking advantage of the unique features of the retina that permit visualization of the central nervous system and micro-vascular circulation through non-invasive approach. Deep learning techniques such as convolutional neural networks (CNNs), have demonstrated their ability to effectively detect features in retinal im-ages that are linked to cardiovascular risk factors [10]. These techniques can support early detection and risk assessment for cardiovascular diseases (CVDs) by extracting significant biomarkers from retinal fundus photography [11]. The Support Vector Machine (SVM) is the best machine learning algorithm that can be used in predicting CVDs using retinal image [13].

It's interesting to note that hybrid machine-learning approaches are extensively used in some studies to enhance prediction accuracy. Decision tree (DT) and Ada Boosting methods can be applied in combi-nation which can help us in predicting coronary heart diseases. [12]. By measuring accuracy, True Posi-tive Rate (TPR), and precision, this hybrid approach seeks to improve the prediction model's perfor-mance. In summary, machine learning algorithms, especially deep learning models and hybrid models which is an amalgamation of more than one machine learning approaches, have produced promising outcomes in predicting CVDs using retinal images. These techniques can be used to achieve disease forecasting and personalized care in a more precise, accurate manner with non-invasive approach [10].

However, further research and clinical validation in real- world scenarios are essential to fully harness the potential of AI in this domain and address existing challenges and limitations in medical applica-tions [13].

III. LITERATURE SURVEY

A systematic scoping review of paper [1] identifies 24 studies that use deep learning approaches on retinal fundus images to predict cardiovascular risk markers and diseases, emphasizing the prevalence of cross-sectional designs and the need for convolutional neural networks and there is a need for more future research in this domain and code sharing.

The review included searching MEDLINE and Embase for peer- reviewed articles and highlighting that there was no external validation of the predictive mod-els, A gap in the robustness and generalizability of findings across different populations can be ob-served with only 21% of the studies performing this validation. The authors suggest the need for multi-modal models combining fundus images with clinical data and suggest a better focus on calibration metrics beyond discrimination.

The study in paper [2] majorly focuses on detecting retinal abnormalities, such as constriction and tor-tuosity, using deep learning techniques like VGG-16 and RESNET-

50. It aims to predict cardiovascular disease by analyzing retinal fundus images and calculating the Ar-teriolar to Venular Diameter Ratio (AVR), a known predictor of cardiovascular risk. AVR is calculated by extracting vessel

diameters and then based on it AVR is computed. The authors confirm that Low AVR values were consistently linked to higher CVD risk.

In Paper [3], the authors highlight that Atherosclerotic Cardiovascular Disease is a leading cause of global hospitalization and mortality. Traditional risk assessment tools like the Pooled Co-hort Equation (PCE) and the Framingham Heart Study, endorsed by the American Heart Association (AHA), have enhanced risk prediction by incorporating clinical and demographic factors to estimate 10-year ASCVD risks (e.g., myocardial infarction, stroke). The human retina, offering a non-invasive view of microvascular health, has been linked to cardiovascular disease, with studies showing correla-tions between retinal microvascular changes (e.g., vessel diameter, tortuosity) and ASCVD risk. Early attempts at automated cardiovascular risk detection using retinal images yielded moderate results, but advancements in deep learning (DL) have improved accuracy. Diabetes-specific adjustments further enhanced model applicability for diabetic populations. However, while the model performed well in older individuals (>60 years), its accuracy was lower in younger populations. A study [4] proposed a methodology for predicting cardiovascular diseases (CVD) using retinal images. The approach in-volved collecting retinal images from individuals with known CVD risk factors like hypertension, diabe-tes, and smoking. Preprocessing techniques, including normalization, denoising, and contrast adjust-ment, were applied to enhance image quality. Segmentation methods were employed to extract essential retinal structures like blood vessels and the optic disc. A convolutional neural network with hierar-chical feature extraction, transfer learning, and stochastic gradient descent was employed for model training. The model's performance was evaluated using accuracy, specificity, sensitivity, and AUC-ROC, achieving an accuracy of 80%. The study highlighted the need for improving model generalizabil-ity, interpretability, and usability in real-world applications as future work.

The connection between diameter of retinal vessel and cardiovascular risk factors is emphasized in Paper [5], which is already a well-known fact. The retinal vascular bed can be used to identify micro-circulation alterations that results in cardiovascular disorders. A more accurate assessment of vascular changes in retina has been achieved by the development of advanced retinal vascular imaging technol-ogies. By incorporating AI into clinical practice, it can improve accuracy of diagnosis and patient care by complementing the role of doctors.

The study in paper [6] investigates the application of various supervised machine learning algorithms like Decision Trees, Support Vector Machines, Logistic Regression, Random Forest, KNN, Naïve Bayes, etc., for predicting heart disease. Using an ensemble approach will improve prediction accuracy. Addi-tionally, incorporating further patient information into the model will help to achieve certain goals re-garding the performance of the model, primarily its robustness. The authors have analysed and com-pared the algorithms to help select the one that achieves the most accurate prediction. An analysis of performance is evaluated in terms of effectiveness, efficiency, recall, F1 score, and the ROC curve-AUC measures.

Paper [7] states that analysis of retinal vessels in fundus images can be carried out in five stages. Name-ly: segmentation of vessels, selection of the region of interest, feature extraction for each vessel, classi-fication of the feature vectors, and finally, a combination of the results for final vessel labelling.

In paper [8], the authors investigate the association between retinal vessel calibres and the occurrence of myocardial infarction (MI). Statistical analyses are carried out to examine the connection between retinal measurements and incident MI. Found a significant association between them and proposed that incorporating DL-derived retinal measurements into existing risk models improved the models' ability to discriminate between patients who did and did not experience an MI.

Paper [9] focused on developing CNN model to measure arteriolar and venular widths of retinal vessels automatically and the system was trained to segment retinal vessels and classify them. The connection between retinal-vessel calibre and CVD risk factors was analyzed using multivariable regression mod-els and the system's predictions were compared with traditional CVD risk assessment tools, such as the Framingham Risk Score, to evaluate its added value. The predictive performance of the system was evaluated for major adverse cardiovascular events including stroke and heart attack.

New developments in AI algorithms and using retinal images to predict systemic disease are presented in paper [10]. The analysis is performed on large datasets of retinal images that are linked to systemic diseases and are broadly representative of the general population. Retinal images are primarily ana-lyzed using CNNs, where pre-trained models such as RESNET, and Inception are fine-tuned in order to improve performance.

A comprehensive survey on deep learning approaches for cardiovascular disease risk evaluation using retinal images is carried out in paper [11]. CNNs is applied in the analysis of retinal images, where fea-tures of retinal image such as retinal vessel calibre, tortuosity, other pathological signs are extracted which are associated with CVD risk factor like atherosclerosis, hypertension and major adverse cardio-vascular evets (MACE). It ensures the high predictive capability of the deep learning models and their viability in such prediction which is safe, cost-affording, and non- invasive.

In paper [12], authors proposes that hybrid models that combines multiple algorithms for prediction of heart diseases performs excellent over individual algorithms by giving prominence to feature selection role and data preprocessing that results in high improved accuracy and robustness. Paper discusses ap-plication of combination of ensemble learning methods with conventional ML models such as Random Forest, Support Vector Machines and Gradient boosting on clinical and demographic features such as hypertension, age and cholesterol levels. The study concludes that hybrid ML approaches are more effective than individual algorithms for heart disease prediction and can be integrated into clinical de-cision-support systems for early diagnosis and risk assessment.

Paper [13] thoroughly examines the implementation and efficacy of AI technologies in medical diagno-sis and disease prediction. The research evaluates various artificial intelligence approaches, including Deep Learning and Machine Learning algorithms, within healthcare settings, emphasizing their preci-sion, performance, and capacity to enhance patient care outcomes. Overall, the investigation offers a thorough evaluation of artificial intelligence's impact on disease diagnosis and prediction, highlighting its revolutionary potential while addressing the obstacles that need to be overcome for widespread in-tegration in the medical field.

The importance of analyzing Optical Coherence Tomography (OCT) images and application of machine learning in diagnosing retinal diseases are discussed in paper [14]. By using OCT, high-resolution cross- sectional images of retina can be fetched which helps us in identifying diseases such as diabetic retinopathy, glaucoma, age-related macular degeneration (AMD), and macular edema. The study em-braces the use of machine learning algorithms such as Decision Trees, SVM, Random Forest which are supervised learning methods and CNNs, attention-based models in automating OCT image analysis and suggests that using these approaches cup-disk ratio can be extracted, drusen and retinal layer thickness which are considered to be major biomarker of CVDs.

Application of machine learning techniques in analyzing ophthalmic data is thoroughly carried out by authors of paper [15] emphasizing the role of these techniques in diagnosing and treating eye condi-tions such as diabetic retinopathy, glaucoma, age-related macular degeneration (AMD), and retinopa-thy of prematurity and authors claim that convolutional neural networks (CNNs) proved to be with highest accuracy in classifying diabetic retinopathy and segmenting retinal layers in OCT scans.

Paper [16][24] provides a detailed review and comparison of various techniques that are employed in retinal vessel segmentation, a critical task in detecting and monitoring eye diseases such as diabetic retinopathy, glaucoma, and hypertension. Authors stress importance of Retinal vessel segmentation for analyzing the structure and condition of blood vessels in the retina that can indicate systemic and ocu-lar diseases. Retinal vessel analysis, incorporating metrics like CRAE, CRVE, and AVR, serves as a valuable predictor of cardiovascular disease by utilizing microvascular biomarkers. AI-driven tools such as QUARTZ and SIVA-DLS improve diagnostic precision, facilitating early risk assessment, pri-mary prevention, and treatment monitoring in cardiovascular health [26].

In paper [17][18], the authors use the UCI Heart Disease dataset that contains attributes such as age, sex, chest pain type, hypertension, cholesterol levels, and other clinical parameters. The paper evalu-ates and compares the performance of several machine learning algorithms such as Logistic Regression, Naïve Bayes, SVM, k-NN, Decision Tree and Random Forest for CVD prediction. The study finds that Random Forest (RF) outperforms other algorithms in terms of accuracy and robustness for CVD predic-tion. The same dataset is used by authors of paper [19] and utilized the Random Forest and K-Nearest Neighbor (K-NN) algorithms on the UCI Heart Disease dataset to classify individuals as having or not having heart disease. The results demonstrated that K-NN achieved an accuracy of 86.885%, outper-forming the Random Forest model, which obtained 81.967% accuracy. The study emphasizes the po-tential of ML-based predictive models in healthcare and suggests further enhancements in feature se-lection and algorithm optimization to improve accuracy.

Paper [20] demonstrated that deep learning models can predict cardiovascular risk factors from retinal fundus images. Using a dataset of 284,335 images from 48,101 patients, a convolutional neural network (CNN) achieved high accuracy, with an MAE of 3.26 years for age and an AUC of 0.97 for gender. The study identified retinal features linked to cardiovascular risk, emphasizing the potential of retinal imag-es as a non-invasive tool for cardiovascular risk assessment. While promising, the approach requires further validation in prospective studies to confirm its clinical utility. This work underscores the role of deep learning in extracting clinically relevant insights from routine eye exams.

Paper [21] proposed a rotation-oriented collaborative self-supervised learning paradigm for diagnosis of retinal disease, addressing the challenge of limited labelled data in medical imaging. The method uses a rotation prediction pretext task (predicting image rotation angles: 0°, 90°, 180°, 270°) to learn meaningful features from unlabeled retinal images. A dual-network architecture (primary and auxiliary networks) collaboratively refines feature learning through pseudo-labeling. The model, pre-trained on unlabeled data, is fine-tuned for

downstream tasks like diabetic retinopathy and macular edema classi-fication. Evaluated on the Messidor- 2 and IDRiD datasets, the approach achieved state-of-the-art per-formance, demonstrating high accuracy, specificity and sensitivity. This work highlights the capability of self- supervised learning to reduce dependency on labelled data while improving diagnostic accura-cy in retinal imaging.
A hybrid model comprising of supervised SVM classification and unsupervised K-means clustering is proposed for retinal blood vessel extraction in paper [22]. Combination of texture, morphological and intensity-based features are used to enhance segmentation accuracy. Proposed techniques assure good performance across different imaging conditions with accuracies of 95.33% and 95.67% tested on standard datasets, namely DRIVE and STARE respectively. The combination of both supervised and unsupervised methods stresses the need of having labelled data, which makes it more suitable for clini-cal applications such as diagnosis of retinal disorders and systemic diseases.
A hybrid model of combining mayfly optimization (MOA) technique and CNN is proposed in paper [23] where MOA helps in optimization of CNNs hyperparameters that results in better performance and faster convergence. The model is evaluated on publicly available retinal image datasets and the performance of the proposed system is measured using metrics such as precision, accuracy, specificity, sensitivity, F1-Score and AUC. The authors conclude that the combination of mayfly optimization and CNN offers a reliable, robust, effective and efficient solution for the retinal image classification with potential applications in clinical practice for early and precise diagnosis of retinal disorders.
Application of different CNN architectures such as EfficientNEtB0 and B7 over retinal fundus images are explored by authors of paper [25]. An automated system for heart disease prediction model using CNN(HDP-CNN) is introduced by researchers. Contrast Limited Adaptive Histogram Equalization (CLAHE) and focal loss are used to enhance image clarity. The model ensures 84% of validation accu-racy highlighting the potential of using this model in early detection of CVD.
The study in paper [28] formulates a novel approach of combining ensemble voting classifier amal-gamating with algorithms like Naïve Bayes, CNNs and Random Forest to capitalize on their strengths. The proposed model achieves a prediction accuracy of 92% which is a remarkable improvement in prediction of coronary artery diseases (CAD). Imbalanced dataset issues were addressed with Synthetic Minority Over-sampling Technique (SMOTE) while Feature selection optimization is ensured using Chi- square test. Robust generalization across diverse datasets and highlights the potential of this ground breaking methodology in early detection of CAD and opens avenues of applying similar techniques in other CVD risk factors.
A multi-modal Ai framework for accurate prediction of cardiovascular disease (CVD) using retinal im-age is proposed in paper [29]. Model is put into practice in four stages, namely – enhancement of image quality and preprocessing techniques, precise segmentation using Entropy-based Fuzzy C Means (EnFCM), feature extraction and selection using Multi-modal Blotzman machine and Genetic algo-rithm, finally classification is performed using ZFNet CNNs. Model is tested across five different da-tasets collected in Qatar region and achieves an exceptionally better performance with an accuracy of 95.89%, specificity of 98.7% and sensitivity of 96.89%. Authors suggests future exploration of addi-tional imaging modalities and scalability with diverse datasets.

IV. COMPARATIVE ANALYSIS

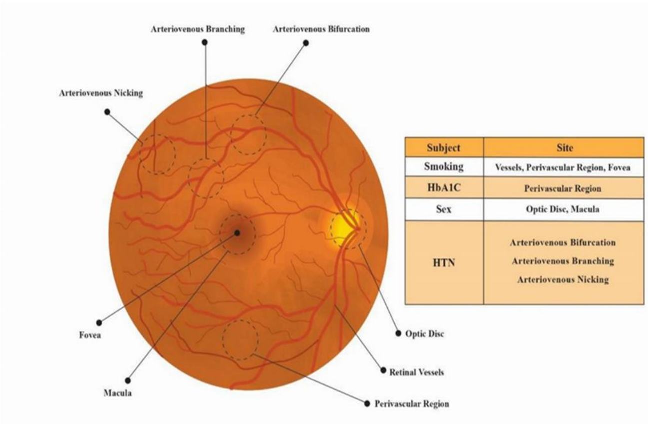

Fig. 1: Features of retina and respective subject of interest that can be extracted from Retinal image

TABLE I: COMPARATIVE ANALYSIS OF DIFFERENT METHODOLOGIES USED AND ACCURACY ACHIEVED

Authors	Features Extracted	Data Sets Used	Methodologies Used	Accuracy achieved
Yashwin P. Prakash, Boora Siri et al.,	AVR	Dataset of retinal fundus images of patients with and without cardiovascular diseases.	VGG-16 and ResNet-50: Used for classification and feature extraction. UNET-based CNN: Used for segmenting retinal blood vessels (arteries and veins).	VGG-16 achieved 97% accuracy, outperforming ResNet-50 (95.32%)
Ehsan Vaghefi et al.,		UK Biobank for training and validation, EyePACS for testing.	Image Preprocessing and Quality Control and Feature Extraction: CNN-based model	
Prasanna Kumar K, H.R. Manjunath et al.,	blood vessels, optic disc, and macula	Local Data	CNN is used for model development. Transfer learning is applied to enhance model performance. Stochastic gradient descent for training the model.	80% achieved
Raluca Eugenia Iorga, Damiana Costin et al	CRAE, CRVE, AVR		QUARTZ-analyses vessel topology SIVA-DLS – measures CRAE/CRVE for cardiovascular risk prediction.	Moderate accuracy achieved – AUC (~0.70 – 0.83)
Yiu Lun Wong, Marco Yu et al.	CRAE, CRVE.	UK BIOBANK Cohort	SIVA-DLS	AUC - 0.745 in age- gender-adjusted models and 0.787 in ultivariable models
Ujwalla Gawande et al.,		EyePACS, Kaggle dataset	EfficientNet, ResNet,VGG, DenseNet, MobileNet, CLAHE	EfficientNetB4 achieved the best validation accuracy (84%)
Ali, M . M.,Quinn et al.,		Standard Dataset	Logistic Regression, Random Forest, Decision Trees, SVM, k- NN, Naive Bayes	
Yiu Lun Wong et al.,	Retinal Vessel calibre	UK BioBank	SIVA (Singapore I Vessel Assessment)	
Cheung CY	Retinal-vessel calibre(arteriolar and venular width) CRAE and CRVE	UK Biobank and SEED	CNN architecture	AUC-ROC of 0.73–0.75
Tan, Y. Y., Lee et al.,	blood vessel patterns, retinal layer thickness	Large cohorts	CNNs, ResNet and Inception	AUC-ROC and C-index.
Barriada et al.,	Vessel calibre, tortuosity	UK Biobank, EyePACS, and MESSIDOR	CNNs (e.g.,U-Net, ResNet, Inception) and transfer learning	AUC-ROC. Accuracy, Sensitivity and Specificity
Katari, S., Rachapudi et al.,		UCI Machine Learning Repository (e.g., the Cleveland Heart Disease dataset).	Random Forest, SVM, and Gradient Boosting.	Accuracy > 90%, Sensitivity > 85%, Specificity > 88%
Imran, A., Pei	Retinal Vessel Segmentation	DRIVE, STARE, and CHASE_DB1	k-means clustering, SVMs, and random forests. U-Net	
Dinesh K.G., Arumugaraj et al.,	Chest pain type, age, sex, cholesterol levels, blood pressure	UCI Heart Disease dataset	Logistic Regression, SVM, k-NN, Naive Bayes, Decision Tree, Random Forest	Accuracy, F1-score, precision, ROC curve analysis.
Garg, Khan et al.,		Heart Disease UCI dataset from Kaggle	k – NN, Random Forest	Accuracy: K -NN – 86.885% Random Forest – 81.967%
Poplin, R., Peng et al.,	changes in blood vessels and optic disc features.	UK Biobank and EyePACS	CNN, Inception-v3 architecture	MAE for regression, AUC for classification. Age: -MAE: 3.26 years. Gender: -AUC: 0.97. Smoking status: - AUC: 0.71. Systolic blood pressure: - MAE: 11.23 mmHg.
Li, X., Xing, L et al.,		Messidor2 and IDRi D	CNN	Accuracy, Sensitivity, Specificity, and AUC.
Hashemzadeh, M et al.,	Retinal blood vessel extraction	DRIVE and STARE	Hybrid model comprising of K- means clustering and SVM	DRIVE dataset (95.33% accuracy and an AUC of 97.12%) STARE dataset (accuracy 95.67% and an AUC of 97.45%.)

Gupta, Choubey, A et al.,		Publicly available retinal fundus image datasets	Hybrid Model (MOA + CNN)	Accuracy, Specificity, Sensitivity, Precision, AUC, F1-Score
WongYL,Yu M et al.,	CRAE, CRVE	UK BIOBANK	CNN	
Mansoor CMM, Chettri SK et al.,		Alizadeh Sani dataset	SVM, CNN, RNN, Random Forests, and Gradient Boosting	Accuracy, Sensitivity, Specificity, Precision, F1-Score, AUC Accuracy of 92%

A comprehensive literature survey is carried out to understand the features of retina that helps us in understanding the risk factors of cardiovascular diseases and are as shown in Figure 1. It is found that Retinal Vascular changes such as Arteriolar narrowing, Venous Dilation, abnormalities in Arteriole-to-Venule Ratio, Tortuosity, Retinal vein occlusion are all associated with Hypertension which is consid-ered as major risk factor of CVD. These features can be extracted from retinal image with the help of various Machine Learning methods. A comparative analysis of features that are extracted and method-ologies used and performance metrics used to measure accuracy achieved are summarized in Table 1.
Ample ways of machine learning approaches are there to predict the possibility of cardiovascular dis-eases using features extracted from retinal image. Researchers used different approaches to achieve this. Accuracy achieved under each of these approaches are summarized in the Figure 2.

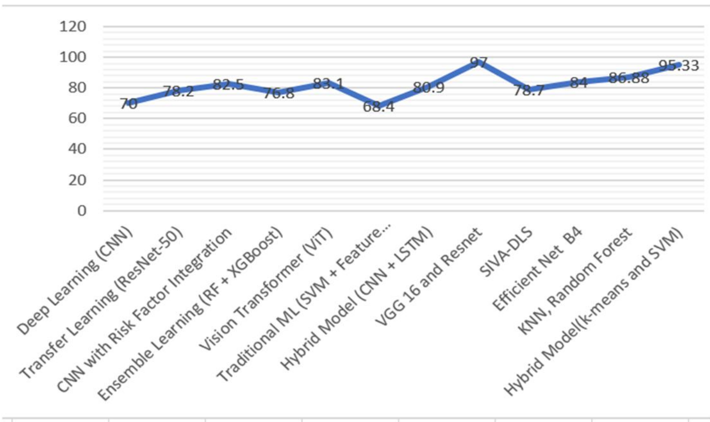

Fig. 2: Approaches used Vs Accuracy achieved

V. Research Gap

Majority of researches carrying out in recent days are relying on the standard data sets that are collect-ed from European populations which is limiting the capability of generalizability of research outcomes across ethnically and racially diverse groups. For example, UK Biobank dataset preponderantly com-prises of non-Hispanic White participants (almost 96%) raising concerns about the relevance of the models to more diverse populations. EyePACS 10K is another such dataset frequently used for external validation predominantly comprises of Hispanic individuals with diabetes, again fails to prove findings of research as generalized across diverse datasets. Hence, to ensure generalizability, there is a critical need for having diverse datasets covering wide range of racial and ethnic backgrounds [3][4][5][8]. This ensures fairness and accuracy. The performance of the predictive systems will vary across populations of different ethnicities or comorbid patients as anatomical structure of these populations are different, highlighting the importance of having diverse dataset.
AI-based retinal analysis tools, such as QUARTZ and SIVA-DLS, show promise but require further val-idation across diverse populations to enhance their generalizability and robustness [3][4]. While cur-rent studies have largely focused on retinal vessel calibre, other retinal features—such as hemorrhages, exudates, and vessel tortuosity—could also play a significant role in predicting cardiovascular disease (CVD) risk [9]. However, several challenges remain, including addressing data diversity, improving model interpretability, and facilitating clinical integration [11]. Technical challenges, such as pro-cessing low-quality images, accurately segmenting thin or overlapping vessels, and achieving real-time performance, further complicate the development of robust AI systems [16].
Additional concern is the imbalance observed in retinal image datasets which contain very fewer posi-tive cases than negative cases, that leads to biased prediction [25]. Different studies have used different methods such as

optical coherence tomography angiography (OCTA), adaptive optics and fundus pho-tography resulting in inconsistencies in retinal vessel measurements. Hence standardization of the da-taset along with retinal imaging techniques are of major concern [5][25]. Absence of universal guide-lines further worsens the prediction capabilities.

VI. FUTURE RESEARCH DIRECTIONS SUGGESTED BY THE PAPER

A significant proportion of contemporary research mainly focused on retinal vessel calibre extrac-tion [8]. However, the direction of future inquiries should be broadened to encompass additional retinal parameters, including vessel tortuosity and arteriovenous nicking. Such an expansion of focus is anticipated to provide a deeper understanding of the correlations between these parameters and cardiovascular risk factors. Furthermore, datasets from different diversity and different health back-ground need to be collected to ensure heterogeneity in dataset and hence achieving generalizability of prediction model which might result in improved prediction capabilities and accuracy [9][15]. Also, different ensemble methodologies need to be explored in order to improve the accuracy of predic-tions associated with retinal vessel parameters [16].

A study about the impact of our lifestyle, age, gender, ethnicity etc., on retinal vascular changes and their association with cardiovascular diseases need to be carried out to provide deeper insights into retinal health and systemic vascular conditions interplay.

REFERENCES

[1] Livie Yumeng Li, Anders Aasted Isaksen et al., “Prediction of Cardiovascular Markers and Diseases Using Retinal Fundus Images and Deep Learning: A Systematic Scoping Review”, European Heart Journal - Digital Health, Volume 5, Issue 6, November 2024, Pages 660 – 669,

[2] Yashwin P. Prakash, Boora Siri et al., “Identifying the Abnormalities in Retinal Images Towards the Prediction of Cardiovascular Disease Using Deep Learning”, International Conference on Wireless Communications and Signal Processing and Networking,IEEE,

[3] Ehsan Vaghefi et al., “Development and Validation of a Deep- Learning Model to Predict 10-Year Atheroscle-rotic Cardiovascular Disease Risk from Retinal Images Using the UK Biobank and EyePACS 10K Datasets”, Cardiovascular Digital Health Journal Volume 5, Issue 2, April 2024, Pages 59-69, Science Direct (Else-vier)

[4] Prasanna Kumar K, H.R. Manjunath et al., “Retinal Image Analysis for Cardiovascular Risk Prediction: A Deep Learning Perspective”, International Journal for Multidisciplinary Research, Volume 6, Issue 3, May-June2024.

[5] Raluca Eugenia Iorga, Damiana Costin et al, “Non-Invasive Retinal Vessel Analysis as a Predictor for Cardi-ovascular Disease”.

[6] Ali, M. M., Quinn, J. M. W., Moni, M. A., Paul, B. K., Ahmed, K., & Bui, F. M. (2021). “Heart disease pre-diction using supervised machine learning algorithms: Performance analysis and comparison.” Computers in Biology and Medicine, 136, 104672.

[7] Miri, M.; Amini, Z.; Rabbani, H.; Kafieh, R. “A Comprehensive Study of Retinal Vessel Classification Meth-ods in Fundus Images”. J.Med. Signals Sens. 2017, 7, 59–70.

[8] Yiu Lun Wong, Marco Yu et al.,”Association between deep learning measured retinal vessel calibre and incident myocardial infarction in a retrospective cohort from the UK Biobank” 2024, BMJ Open Volume 14, Issue 3

[9] Cheung CY, Xu D, Cheng C-Y, et al. “A deep-learning system for the assessment of cardiovascular disease risk via the measurement of retinal-vessel calibre.” Nat Biomed Eng 2021; 5:498508.

[10] Tan, Y. Y., Lee, C. J., Thakur, S., Tham et al., (2024). “Prognostic potentials of AI in ophthalmology: systemic disease forecasting via retinal imaging”. Eye and Vision, 11(1).

[11] Barriada, R. G., & Masip, D. (2022). “An Overview of Deep- Learning-Based Methods for Cardiovascular Risk Assessment with Retinal Images”. Diagnostics, 13(1),68.

[12] Katari, S., Rachapudi, V., Sree, M. P. S., & Likith, T. (2023). “Heart Disease Prediction using Hybrid ML Algorithms”. 121–125.

[13] Ghaffar Nia, N., Nasab, A., & Kaplanoglu, E. (2023). “Evaluation of artificial intelligence techniques in dis-ease diagnosis and prediction.” Discover Artificial Intelligence,3(1).

[14] Karn, P. K., & Abdulla, W. H. (2023). “On Machine Learning in Clinical Interpretation of Retinal Diseases Us-ing OCT Images”. Bioengineering,10(4),407.

[15] Sarhan, M. H., Nasseri, M. A., Zapp, D., Eslami, A., Lohmann, C. P., Navab, N., & Maier, M. (2020). “Machine Learning Techniques for Ophthalmic Data Processing: A Review. IEEE Journal of Biomedical and Health Informatics”.

[16] Imran, A., Pei, Y., Wang, Q., Yang, J.-J., & Li, J. (2019). “Comparative Analysis of Vessel Segmentation Tech-niques in Retinal Images”. IEEE Access, 7, 114862–114887.

[17] Dinesh, K. G., Arumugaraj, K., Mareeswari, V., & Santhosh, K. D. (2018). “Prediction of Cardiovascular Dis-ease Using Machine Learning Algorithms”. 1–7.

[18] Princy, R. J. P., Parthasarathy, S., Raj Lakshminarayanan, A., Hency Jose, P. S., & Jeganathan, S. (2020, May 1). “Prediction of Cardiac Disease using Supervised Machine Learning Algorithms”.
[19] Garg, A., Khan, R., & Sharma, B. (2021). “Heart disease prediction using machine learning techniques. IOP Conference Series: Materials Science and Engineering”, 1022(1), 012046.
[20] Poplin, R., Peng, L., Liu, Y., Corrado, G. S., Webster, D. R., Varadarajan, A. V., Blumer, K., & Mcconnell, M. V. (2018). “Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning.” Na-ture Biomedical Engineering, 2(3),158–164.
[21] Li, X., Xing, L., Hu, X., Yu, L., Zhao, W., Heng, P.-A., & Qi, X. (2021). “Rotation-Oriented Collaborative Self-Supervised Learning for Retinal Disease Diagnosis. IEEE Transactions on Medical Imaging”, 40(9), 2284–2294.
[22] Hashemzadeh, M., & Adlpour Azar, B. (2019). “Retinal blood vessel extraction employing effective image fea-tures and combination of supervised and unsupervised machine learning methods”. Artificial Intelligence in Medicine,95,1–15.
[23] Gupta, I. K., Choubey, A., & Choubey, S. (2022). “Mayfly optimization with deep learning enabled retinal fundus image classification model”. Computers and Electrical Engineering, 102,108176.
[24] Amini, Z., Miri, M., Kafieh, R., & Rabbani, H. (2017). “A Comprehensive Study of Retinal Vessel Classifica-tion Methods in Fundus Images”. Journal of Medical Signals & Sensors, 7(2), 59.
[25] U. Gawande et al., "Efficient Heart Disease Risk Management: A CNN-based Approach for Automated Predic-tion using Retinal Fundus Image," 2024 1st International Conference on Advanced Computing and Emerging Technologies (ACET), Ghaziabad, India, 2024, pp. 1-6.
[26] Iorga RE, Costin D, Munteanu-Dănulescu RS, Rezuș E, Moraru AD. “Non-Invasive Retinal Vessel Analysis as a Predictor for Cardiovascular Disease”. J Pers Med. 2024 May 9;14(5):501.
[27] Wong YL, Yu M, Chong C, Yang D, Xu D, Lee ML, Hsu W, Wong TY, Cheng C, Cheung CY. “Association between deep learning measured retinal vessel calibre and incident myocardial infarction in a retrospective co-hort from the UK Biobank”. BMJ Open. 2024 Mar 21.
[28] Mansoor CMM, Chettri SK, Naleer HMM. “Development of an efficient novel method for coronary artery dis-ease prediction using machine learning and deep learning techniques”. Technol Health Care. 2024;32(6):4545-4569.
[29] Gurumurthy, P., Alagarsamy, M., Kuppusamy, S., & Ponnusamy, N.C. (2024).M2AI-CVD: “Multi-modal AI approach cardiovascular risk prediction system using fundus images”. Network: Computation in Neural Sys-tems, 35(3), 319–346.