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RESEARCH ARTICLE

Systematic Development of AI-Enabled Diagnostic Systems for Glaucoma and Diabetic Retinopathy

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ABSTRACT With the rapid advancements in artificial intelligence, particularly in machine learning and deep learning, automated disease diagnosis is becoming increasingly feasible. Generating larger databases is crucial for training and validating the performance of models for chronic diseases such as glaucoma and diabetic retinopathy, which progress slowly and unnoticed. Automated procedures for retinal vessel segmentation and optic cup/disk localization are preferred for large-scale screening of the public, contributing to the early detection and treatment of eye diseases, preventing blindness, and improving public health. This paper focuses on the challenges involved in segmenting the retinal vessels from fundus images and presents a modified ColonSegNet model for retinal vessel segmentation that includes efficient methods for locating the true vessels and applies data augmentation to overcome the issue of fewer graded images. The paper uses the optimal values for the contrast enhancement of retinal fundus images using intelligent evolution algorithms. The central vessel reflex, bifurcation, crossover, thin vessels, and lesion presence are highlighted as significant challenges in retinal vessel segmentation. The proposed method achieves high sensitivity, specificity, and accuracy, {0.839, 0.979, 0.966}, {0.865, 0.979, 0.971}, and {0.867, 0.981, 0.972}, segmenting retinal vessels on DRIVE, CHASE_DB, and STARE. The work is crucial in developing automated systems for the early detection and treatment of eye diseases, thereby improving public health.

INDEX TERMS Deep learning, disease diagnosis, diabetic retinopathy, glaucoma, image classification, retinal vessels, cup to disc ratio.

I. INTRODUCTION

The manual disease diagnosis is almost irreplaceable due to the complications of the diseases and the satisfaction of the patients. But for some diseases and large-scale population-level screening programs of Governments, the automated methods for disease diagnosis are fast, reliable, and preferable. Still, the final check-up and decision about the disease and patient could be made only based on the opinion and suggestions of the medical expert. The automated disease diagnosis methods aim to detect and isolate the suspected cases for manual checks by doctors. These methods will not only isolate the suspected cases but will also assist the medical expert in decision-making in many cases.

The diagnosis of various diseases using automated methods is feasible due to the unparalleled development in the fields of machine/deep learning, big data, and image processing in the last two decades. The electronic health record of the patients along with the symptoms and different modalities of images can easily be maintained in medical databases. Such databases can be used for the training and testing of any developed deep learning (DL) models, which are integrated into automated systems for disease diagnosis/classification.

The authors in [1] proposed an automatic screening system for diabetic retinopathy based on several steps including image pre-processing, detection and removal of optic disc, segmentation and removal of retinal vessel, removal of fovea,

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extraction of lesions such as hemorrhage, micro-aneurysm, exudates etc., selection of important features and classification. They performed simulation using DIARETDB1 retinal image database and validated their achieved results by comparing with manual grading of expert ophthalmologists. They claimed improved evaluation metrics including specificity, sensitivity, and accuracy.

The authors in [2] presented a framework based on SVM and Naïve-Bayes classifiers for processing the retinal image, segmentation of retinal vessel, localization and removal of optic disc, feature extraction and classification of the different bright lesions. They used the publicly available image-Ret database testing their developed framework. The image-Ret is comprised of two sub-databases, which are DIARETDB0, and DIARETDB1. They performed extensive simulation and validated their approach by comparing the achieved evaluation metrics with those of rivals from the literature.

The authors in [3] explored a new approach based on a combination of artificial intelligence and image processing for the diagnosing of diabetes retinopathy based on retinal fundus images. They proposed automatic DR diagnosis based on several stages, where the analysis and simulation has been performed using MATLAB based software. They validated their developed approach by comparing the achieved results with those of expert ophthalmologists. They experimented with detection of different types of lesion including exudates, micro-aneurysms, and retinal hemorrhages, which are the main cause of diabetic retinopathy. Their achieved detection accuracies based on experiments works are more than 98.80%.

Some of the well-known vision-threatening eye diseases are diabetic retinopathy (DR), Glaucoma, and Age-Related Macular Degeneration (AMD). Among the working-age population of the world, DR is one of the vision-threatening diseases, which could be treated if detected timely. This disease is a defect, which occurs in the retinal vasculature of almost all patients with diabetes. Glaucoma is another eye disease (second highest occurring eye disease), which slowly impacts the optic nerve. Not detected and treated promptly can lead to full or partial blindness. AMD is an eye disease causing permanent blindness in adults in advanced countries. This disease is linked with aging, which slowly damages the sharp central vision.

Most eye diseases occur slowly and their symptoms are not significant or observable in the beginning. This makes it more challenging to accurately diagnose such diseases. Hence, such slowly occurring diseases require us to develop automated methods for continuous and large-scale population screening programs. By developing and installing such automated tools/systems at hospital facilities, the diseases of many individuals can effectively be detected in the initial stages.

On the other hand in the current setup, the medical experts (Ophthalmologists) observe the morphological changes manually, which is tired-some and requires significant time on a large scale. Additionally, manual assessment by doctors is prone to error due to the huge burden. Hence, the efficacy of the manual setup for large-scale population screening is significantly lower compared to that of the deep learning-based automated system.

The contributions of the work are as follows:

- Exploration of challenges involved in automated segmentation of retinal vessels and optic cup/disk
- Identification of solutions adapted by researchers for dealing with the different challenges
- Development of DL model by implementing these strategies for the case of retinal vessels segmentation

The organization of the manuscript is as follows. Section I presents the introduction and background knowledge of the various eye diseases. It also presents the significance of AI-enabled diagnostics systems for DR and Glaucoma eye diseases. Section II provides the literature review. The details of the frameworks for AI-enabled eye disease classification are unfolded in Section III. The details of basic model and enhanced model are provided in Section IV. The results and discussion are provided in Section V. The concluding remarks along future directions are provided in Section VI.

A. SIGNIFICANCE OF AI-ENABLED AUTOMATED DIAGNOSTICS SYSTEM FOR EYE DISEASE CLASSIFICATION

Timely diagnosis of diabetic retinopathy and Glaucoma is highly desired, as the suspect does not feel symptoms in the beginning unless the disease progresses to advance stages, where it is irreversible. This makes it more challenging to accurately diagnose such diseases. Hence, such slowly occurring diseases require us to develop automated methods for continuous and large-scale population screening programs. By developing and installing such automated tools/systems at the front desk in hospital, the diseases of many individuals can effectively be detected in the initial stages of the regular check ups for hypertension and diabetes. In this way, the complication of eye diseases in progression to advanced stages could be avoided.

The general symptoms of these eye diseases include lesions such as hard/soft exudates, microaneurysms (MA), intraretinal microvascular problems, blot/dot hemorrhages as well as leakages. The constituents parts of the human retina and some of these diseases are shown in Fig. 1. The lesion shown in Fig. 1 are usually not observable in the initial stages of the diseases until they progress to advanced stages. Mostly, the patients are not aware while their diseases are progressing to advanced stages. The symptoms can only be observed by expert ophthalmologists, who need to carefully examine the retina and grade it by counting the number and size of each type of lesion. Additionally, they need to judge the severity of the lesion [4].

B. GLAUCOMA AND DIABETIC RETINOPATHY

The retina contains many identifiable parts such as the iris, macula, vessels, vitreous, optic cup/disk, pupil, and cornea.

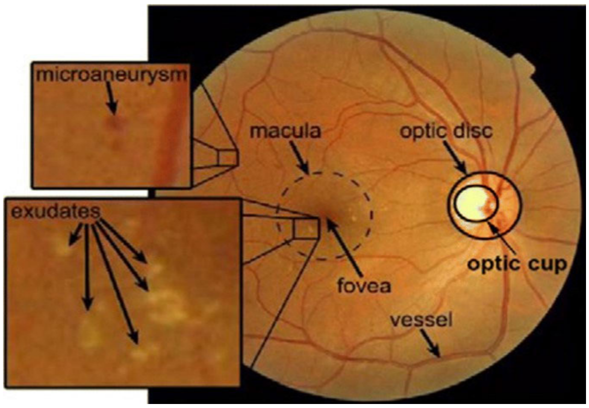

FIGURE 1. The constituents parts of the retina along with exudates and micro-aneurysms.

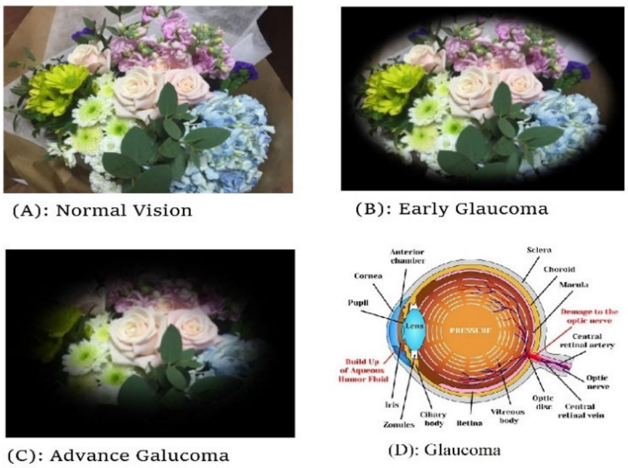

FIGURE 2. The stages of Glaucoma [6].

The observable symptom of the DR is MA, which is caused by the leakage from ruptured vessels. The MA characterizes circular shape and red color. When the disease advances and the walls of MA get ruptured then it results in the formation of Hemorrhages. On the other hand, when the excretion from the blood vessels have proteins and lipids then exudates are created. The exudates can be soft or hard, which results in vision loss if formed around the macula. The exudates are bright in color and hemorrhages characterize dark color [5]. The optic nerve carries impulses, which contain information observed at the retina to the concerned part of the brain for further processing and decision-making.

Glaucoma advances gradually and directly damages the optic nerve due to the pressure imposed on it, which results in vision loss. The main reason behind Glaucoma is the failure of the eye to excrete waste fluid. The accumulated excess fluid generates pressure (intra-ocular) that damages the optic nerve. This extra pressure thickens the layers of retinal nerve fibers, which results in an increased size of the optic cup compared to the size of the optic disk, known as ''cupping''. The Glaucoma stages are shown in Fig. 2 ([6]).

The three stages of non-proliferative DR are shown in Fig. 3 ([7]). The early stage of non-proliferative DR (NPDR) is mild. In this stage of NPDR, small blood vessels are formed inside retinal vessels, which secrets little blood that forms micro-aneurysms (MAs). With time, the disease advances, in which the wall of MAs is ruptured due to which fluid is leaked into the retina. The fluid leakage leads to the formation of exudates and hemorrhages, which is the next stage of the DR called moderate non-proliferative DR. The third stage of non-proliferative DR is severe, which causes the blockage of blood supply in some retinal vessels. In this stage of NPDR, the blood supply to some areas of the retina is affected. Such areas of the retina exude growth factors, which lead to the formation of new retinal blood vessels.

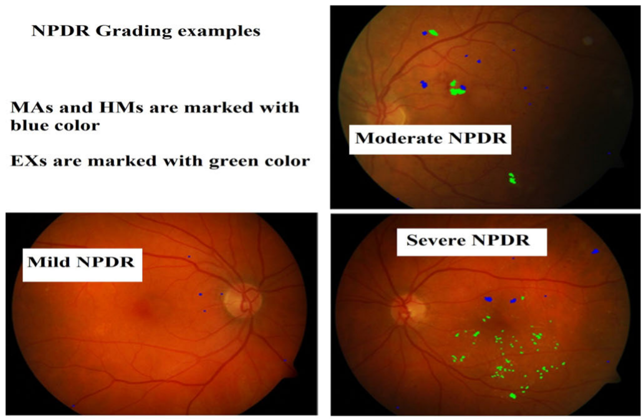

FIGURE 3. The three sub-stages of non-proliferative DR.

II. LITERATURE REVIEW

Numerous eye diseases exist, which can be detected/diagnosed using enhanced DL models trained/tested based on the images in the state-of-the-art retinal image databases. The authors in [8] conducted a review of computer-aided based methods for automated diagnosis of eye diseases, especially glaucoma.

Numerous publicly available retinal image datasets including DRISHTI-GS, RIMONE, DRIVE, STARE, and CHASE-DB are used in many studies for performance evaluation of DNN models. These publicly available retinal image datasets contain images along with the ground truth (gold standards) for both cases with and without diseases. DRISHTI-GS and RIMONE have been used for OD and OC segmentation whereas the other three are used for retinal vessel segmentation. The RIM-ONE [9] is comprised of 159 retinal images, which are publicly available for performance evaluation of the DNN model developed for OD and OC segmentation. Among 159 images, 74 represent Glaucomatous eyes while the remaining represent healthy eyes.

The Drishti-GS [10] database contains 101 retinal images. These images were manually marked by the ophthalmologist at Aravind Eye Clinic in India. The resolution of all these is 2896∗1944, which are saved 9 without compression) in PNG format. The OD and OC are marked in these retinal fundus images.

The DRIVE [3] dataset contains 40 retinal images, which have a resolution of 565 × 584 pixels. The 40 images were distributed into a test set and training set, where each have 20 retinal images. The STARE [11] dataset is comprised of 20 retinal fundus images, which have a resolution of 605 × 700 pixels. Due to very limited graded images, the STARE does not have separate tests and training, where a leave-one-out approach is used. According to this approach, a DNN model is trained on n-1 samples (in this case 19 images) and tested on the left one image. The CHASE_DB [12] database is comprised of 28 retinal images having a resolution of 999 × 960 pixels. Among 28 retinal images, 20 retinal images are used for training the DNN model, and the remaining 8 retinal images are used for testing the developed DNN model.

Machine vision and image processing algorithms provide the basis for modern ophthalmology. In the various constituent parts of the eye, the blood vessels are significantly important and are mostly used for disease diagnosis such as DR [13]. The DR damages the retinal blood vessels of diabetic patients. In worst cases, DR causes blindness in diabetic patients, which can be avoided by detecting it in the early stages and providing proper treatment. But, it is highly challenging to correctly diagnose DR in the early stages because of the unobservable symptoms in early stages [14]. The DR occurs due to the variations in retinal blood vessels that lead to retinal disorder and in the initial stages, the patient complete losses vision.

Mainly, there are two types of DR i.e. proliferative and non-proliferative [14], [15]. In proliferative DR (PDR) new blood vessels are formed, which grow in the inner retinal surface and vitreous gel. These newly created retinal vessels are fragile, which means they are highly likely for blood leakage into the retina. Due to blood leakage from the newly created retinal blood vessels, different kinds of lesions are created, which worsen further and ultimately lead to permanent blindness [16].

The authors in [7] explained the three different stages of non-proliferative DR (NPDR). The first is a mild stage NPDR, in which small blood vessels are formed inside retinal vessels, which secrets little blood that forms micro-aneurysms (MAs). With time, the disease advances, in which the wall of MAs is ruptured due to which fluid is leaked into the retina. The fluid leakage leads to the formation of exudates and hemorrhages, which is the next stage of the DR called moderate non-proliferative DR. The third stage of non-proliferative DR is severe, which causes the blockage of blood supply in some retinal vessels. In this stage of NPDR, the blood supply to some areas of the retina is affected. Such areas of the retina exude growth factors, which lead to the formation of new retinal blood vessels.

The paper [1] proposes an effective image processing method for the detection of diabetic retinopathy diseases from retinal fundus images. The proposed method involves several steps, including pre-processing, feature extraction, and feature selection, and was evaluated on the DIARETDB1 dataset, achieving high efficiency and effectiveness in sensitivity, specificity, and accuracy.

The paper [2] proposes an automated system for detecting exudates and cotton wool spots in early stages of diabetic retinopathy. The proposed method involves processing the retinal image, vessel segmentation, optic disc localization and removal, feature extraction, feature selection, and classification using SVM and Naïve-Bayes classifiers.

In [3], authors presents a new approach for detecting diabetic retinopathy using retinal fundus images, which combines image processing and artificial intelligence. The proposed method involves feature extraction and classification, and achieves high accuracy in detecting various types of diabetic retinopathy, including exudates, micro-aneurysms, and retinal hemorrhages. The proposed method is evaluated using MATLAB simulation and compared to expert ophthalmologists, demonstrating high sensitivity, specificity, and accuracy in detecting the disease.

In [17], paper proposes a new pipeline technique for the automatic diagnosis of brain cancer images from MRI, which involves feature extraction, preprocessing, and an optimal artificial neural network. The improved metaheuristic, courtship learning-based water strider algorithm, is used for feature selection and classification, resulting in higher efficiency compared to other analyzed procedures.

In [18], the authors designed two basic modules, Patches Convolution Attention Transformer (PCAT) and Feature Grouping Attention Module (FGAM). Both are used to extract refined feature maps with multi-scale feature information. These modules work together to integrate feature information from both, achieving complementary functions. The PCAT-UNET approach has proven to be effective in achieving accurate retinal vessel segmentation.

In [19], authors present Genetic U-Net, a novel automated design method. They used an improved genetic algorithm (GA) to identify better-performing architectures in the search space and explore the potential of finding a superior network architecture with fewer parameters. This method achieved better retinal vessel segmentation with fewer parameters.

The paper [20] proposes a new DL pipeline called DR-VNet that combines residual squeeze and excitation blocks with residual dense net blocks. DR-VNet consists of two cascaded sub-networks a Backbone Residual Dense network and a Fine-tune Tail network. The Backbone Residual Dense network and the Fine-tune Tail network are the two cascaded sub-networks that comprise the DR-VNet. Both the thicker and the thinner retinal vessels can be segmented more effectively using this method.

III. THE FRAMEWORK FOR DR AND GLAUCOMA DETECTION

In this section, we discuss the details of the databases used along with the essential tasks required for eye disease classification. Initially, Pre-processing is performed for ensuring that the dimension of all the images is consistent and their contrast is suitable enhanced. The suitable channel is selected and extracted for further processing. Mostly, the researchers select the green channel of the RGB image, which is enhanced using CLAHE. The pre-processing is performed for removing the noise in the image and improving the quality of the image through various transformations including brightness transformation and contrast enhancement [21].

Other than PSO based CLAHE, the well-known pre-processing steps include contrast enhancement based on morphological Top-Hat transformation and filtering. Usually, CLAHE and Top-Hate transformation are applied along with any suitable filtering, for image processing based retinal vessel segmentation. For machine and deep learning based approaches for retinal vessels and optic cup/disk segmentation does not require significant pre-processing. For these approaches, cropping along with data augmentations are used for generating large databases needed for better training and testing of the developed models.

The image resizing is performed using cropping and a suitable interpolation method. The cropping is performed based on the size of the diameter of the field of view (FoV), which in our case is the retina. The contrast enhancement is performed for highlighting the important features in the images. A suitable method mostly selected by the researchers for contrast enhancement of retinal fundus images is CLAHE. The contrast enhancement of retinal fundus images is a basic pre-processing operation, for which the CLAHE has been used with its default parameters in the past [22], [23], [24].

The issue with the default parameters of CLAHE is that it may lead to non-optimal contrast enhancement for some fundus images of any database. The non-optimal contrast enhancement due to default parameters of CLAHE leads to difficulty in accurate segmentation of vascular structure and Optic Cup/Disk in retinal fundus images. In our most recent work in [21], we exhaustively evaluated the impact of CLAHE parameters optimization on the contrast enhancement of retinal fundus images. An advanced version of the optimization process, which we applied in [21] is shown in Fig. 4 that can be applied to any other image database. The researchers may apply any other optimization algorithm other than particle swarm optimization (PSO), which may produce better results or may also reduce the execution time.

An illustrative example of the impact of the optimization process of CLAHE parameters on the contrast enhancement of retinal fundus images is shown in Fig. 5. It is evident from Fig. 5 that the parameter optimization of CLAHE has a significant impact on contrast enhancement of the retinal fundus images. So, it is highly recommended to choose any evolution algorithm for parameter optimization of CLAHE as a pre-processing step before training and testing of any developed DL model.

The retinal blood vessel segmentation and the demarcation of their morphological features including width, length, tortuosity, and branching angles/pattern are important attributes, which can be used for the classification of numerous diseases such as DR, cardiovascular, arteriosclerosis, choroidal neovascularization, and hypertension [25]. Accurate retinal vessel segmentation is a challenging task, which affects the diagnosis of the above-mentioned diseases.

In our recent work in [21], we exhaustively investigated all possible scenarios for the parameters of CLAHE and evaluated its impact on the accuracy of retinal vessel segmentation. We concluded that for accurate retinal vessel segmentation, we need to intelligently explore the optimum parameter values for the contextual region and clip limit of CLAHE. Besides contrast enhancement of fundus images, there are numerous other challenges, which limit the performance of both supervised and unsupervised machine/deep learning models for retinal vessel segmentation.

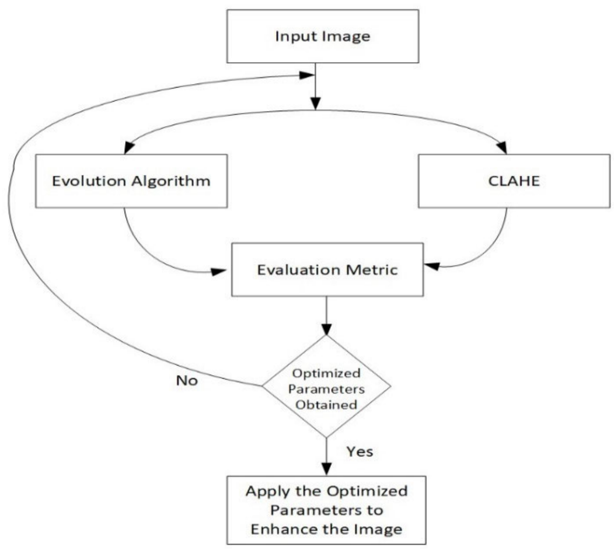

FIGURE 4. Optimization of CLAHE parameters for contrast enhancement of retinal fundus images.

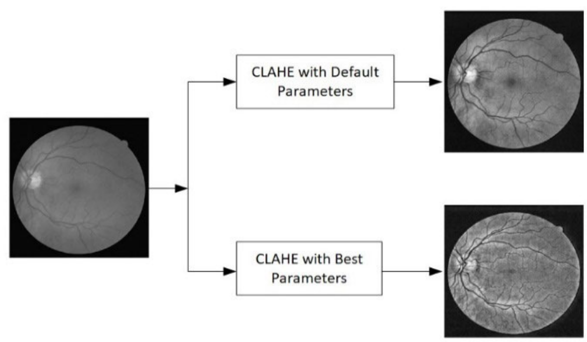

FIGURE 5. The impact of CLAHE parameters optimization on contrast enhancement of retinal image.

In the medical community, it is a widely accepted notion that the automatic segmentation of retinal blood vessels is a very important step for the development of an automated eye disease classification system. Many eminent researchers have developed state-of-the-art algorithms and machine/deep learning models for accurate and reliable segmentation of retinal blood vessels in the last two decades. But there are numerous problems and challenges that need to be addressed by the research community. The various challenges in retinal vessel segmentation are mentioned below [26].

The central vessel reflex is one of the main challenges which hinders accurate retinal vessel segmentation. The bifurcation and crossover are also big challenges, which affect the segmentation accuracy of retinal vessels. The merging point of two or more vessels also affects the segmentation accuracy. The segmentation of thin vessels is also difficult. The presence of various kinds of lesions also has negative impact on segmentation accuracy.

The crossover and bifurcation issues are highlighted graphically in Fig. 6. We have recently explored supervised and unsupervised approaches for accurate retinal vessel segmentation [21], [23], [24], [27]. Some other eminent researchers have also targeted the above mention challenges during retinal vessel segmentation [7], [22], [26].

Despite the better evaluation metrics of the unsupervised and supervised techniques, different issues still require the proper focus of the research community.

The optic cup and disk segmentation is a challenging task, where significantly high accuracy is needed for the diagnosis of Glaucoma. Before the development, training, and assessment of the DL model for accurate optic and optic disk segmentation, we need to explore an efficient strategy for contrast enhancement of the fundus images of the desired databases. The general flow diagram for OD/OC and retinal vessel segmentation using any developed DL model is shown in Fig. 7. One of the major issues with OD detection is the presence of vessels inside it, which hinders its accurate segmentation. The presence of vessels inside OD is shown graphically in Fig. 8 [28].

Furthermore, the post-processing and pre-processing tasks are based on heuristic algorithms, due to which their adjustment to noises and different pathologies is needed. Another issue is the higher computational time and memory requirement of the previously explored DL methods. The higher execution time required for the training of DNN and the tuning of its hyper-parameter limits their deployment for population scale monitoring.

The segmentation of retinal vessels using a lightweight deep neural network model is the primary objective of the present study. Researchers have characterized the segmentation of retinal vessels in retinal fundus images as a challenging task of semantic segmentation, where the individual pixels are identified using a pixel-by-pixel approach.

By carefully examining the earlier studies, it is clear that the missed identification of the tiny vessels in retinal fun had a significant effect on the sensitivity of the previous methods. For segmenting retinal vessels, we currently present a DL model termed RC-DNN. The focus has been on effectively detecting thin vessels in addition to thick blood vessels, which significantly enhances the accuracy of the models.

Most of the previous works on retinal vessel segmentations attribute higher computational complexity and some of them even require some pre and post-processing steps [1], [2], [3], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27]. Additionally, these previous works attribute higher computational complexity to the DL model. Recently, we applied the ColonSegNet [29] model for retinal vessel segmentation, which is lightweight and also achieved significantly lower computational complexity compared to previous attempts for the same task of retinal vessel segmentation. In the current work, we further optimized ColonSegNet Model and achieved even improved results without compromising on the evaluation metrics of the developed model.

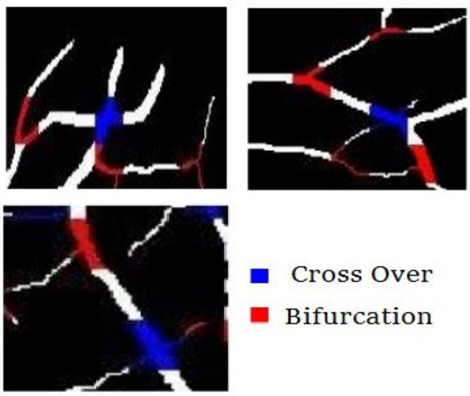

FIGURE 6. Crossover and bifurcation issues.

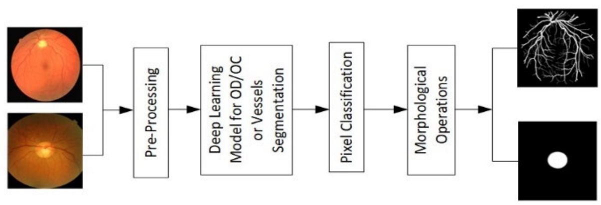

FIGURE 7. The general flow diagram for OD/OC detection and retinal vessels segmentation.

All these challenges, specifically the damage caused by different lesions hinders accurate vessel segmentation. For accurate and reliable vessel segmentation, it is recommended to select suitable pre and post-processing operations, which are faster and assist the developed learning model in achieving better evaluation metrics.

There are numerous challenges in developing AI-based automated solutions for eye disease classification. Accurate retinal vascular segmentation is hampered by a number of issues, one of which is the central vessel reflex. The

TABLE 1. Performance comparison of various models for retinal vessels segmentation on three databases.

Methods	DRIVE			CHASE_DB1			STARE		
	Se	Sp	Acc	Se	Sp	Acc	Se	Sp	Acc
Marin et al.[36]	0.7067	0.9801	0.9452	N.A	N.A	N.A	0.6944	0.9819	0.9526
Fraz et al.[25]	0.7406	0.9807	0.9480	0.7224	0.9711	0.9569	0.7548	0.9763	0.9534
Cheng et al.[37]	0.7252	0.9798	0.9474	N.A	N.A	N.A	N.A	N.A	N.A
Azzopardi et al.[38]	0.7655	0.9704	0.9442	0.7585	0.9587	0.9387	0.7716	0.9701	0.9497
Roychowdhury et al.[39]	0.7395	0.9782	0.9494	0.7615	0.9575	0.9467	0.7317	0.9842	0.9560
Zhang et al.[40]	0.7743	0.9725	0.9476	0.7626	0.9661	0.9452	0.7791	0.9758	0.9554
Li et al.[41]	0.7569	0.9816	0.9527	0.7507	0.9793	0.9581	0.7726	0.9844	0.9628
Yan et al.[42]	0.7653	0.9818	0.9542	0.7633	0.9809	0.961	N.A	N.A	N.A
Jiang et al.[43]	0.7839	0.9890	0.9709	0.7839	0.9894	0.9721	N.A	N.A	N.A
Adapa et al.[44]	0.6994	0.9811	0.945	N.A	N.A	N.A	N.A	N.A	N.A
SS without MPSO-CLAHE [21]	0.8252	0.9787	0.9649	N.A	N.A	N.A	0.8397	0.9792	0.9659
SS with MPSO-CLAHE [21]	0.8315	0.9750	0.9620	N.A	N.A	N.A	0.8433	0.9760	0.9645
PCAT-UNet[18]	0.8576	0.9932	0.9622	0.8493	0.9966	0.9812	0.8703	0.9937	0.9796
Genetic U-Net[19]	0.8300	0.9758	0.9577	0.8463	0.9818	0.9667	0.8658	0.9846	0.9719
DR-VNet[20]	0.8512	0.9795	0.9682	0.9120	0.9733	0.9694	0.8572	0.9841	0.9744
ColonSegNet [29]	0.8491	0.9774	0.9659	0.8607	0.9806	0.9731	0.8573	0.9813	0.9719
ColonSegNet V2 (Proposed)	0.8391	0.9794	0.9669	0.8655	0.9792	0.97199	0.8671	0.9812	0.9723

TABLE 2. Performance of various deep learning models for OD and OC segmentation using DRISHTI-GS.

References	Year	OC				OD			
		F1	**JC**	**Sens**	**Spec**	**F1**	**JC**	**Sens**	**Spec**
Sedai et al.[42]	2016	85	-	-	-	95	-	-	-
Sevastopolsky et al.[45]	2017	85.21	75.15	84.76	98.81	90.43	83.5	91.56	99.69
Zilly et al.[46]	2017	87.1	85	-	-	97.3	91.4	-	-
Fu et al.[47]	2018	86.18	77.3	88.22	98.62	96.78	93.86	97.11	99.91
Son et al.[48]	2019	86.43	77.48	85.39	99.07	95.27	91.85	97.47	99.77
Xu et al.[49]	2019	89.2	82.30	-	-	97.8	94.9	-	-
Gao et al.[32]	2020	90.58	-	-	-	97.87	-	-	-
Tabassum et al.[33]	2020	92.4	86.32	95.67	99.81	95.97	91.83	97.54	99.73
Liu et al.[34]	2021	91.2	84.4	-	-	97.8	95.7	-	-

contrast enhancement of retinal fundus images is the first step required to improve the images. Another significant problem influencing the segmentation accuracy of retinal vessels is the bifurcation and crossing over. The performance of the segmentation algorithm is also influenced by the point at which two or more vessels join. Tiny vessel segmentation is also troublesome. Accurate segmentation is also negatively impacted by the presence of numerous red pathologies that exists in images of the diseased retina.

One of the main issues is the computation time of the post-processing and pre-processing operation, which increases the computational complexity of the overall system. Furthermore, the DL model for retinal vessel segmentation attributes a significant number of hidden layers, which

TABLE 3. Performance of various deep learning models for OD and OC segmentation using RIM-ONE.

References	Year	OC				OD			
		F1	JC	Sens	Spec	F1	JC	Sens	Spec
Sevastopolsky et al.[45]	2017	82	69	75.45	99.76	95	89	95.02	99.73
Arnay et al.[50]	2017	-	75.7	-	-	-	-	-	-
Zilly et al.[46]	2017	82.4	80.2	-	-	94.2	89	-	-
Fu et al. [47]	2018	83.48	73	81.46	99.67	95.26	91.14	94.81	99.86
Son et al.[48]	2019	82.5	71.65	81.42	99.65	95.32	91.22	94.57	99.87
Wang et al.[51]	2019	78.7	-	-	-	86.5	-	-	-
Xu et al.[49]	2019	85.64	75.86	85.15	99.71	95.61	91.72	95.21	99.87
Tabassum et al.[33]	2020	86.22	75.32	95.17	99.81	95.82	91.01	97.34	99.73

FIGURE 8. The challenges in OD and OC detection.

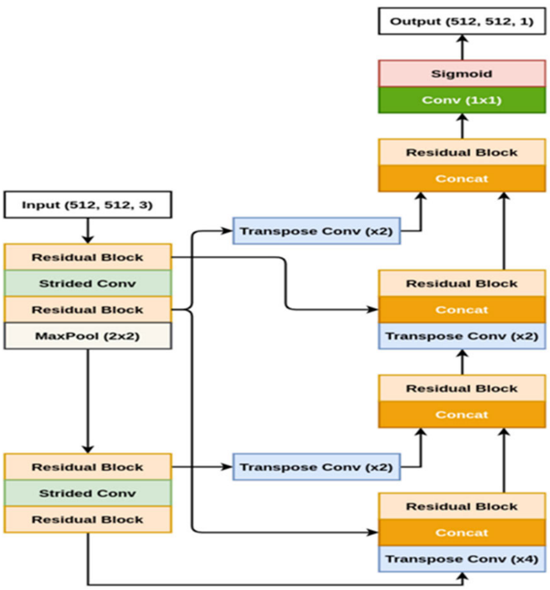

FIGURE 9. ColonSegNet block diagram [30].

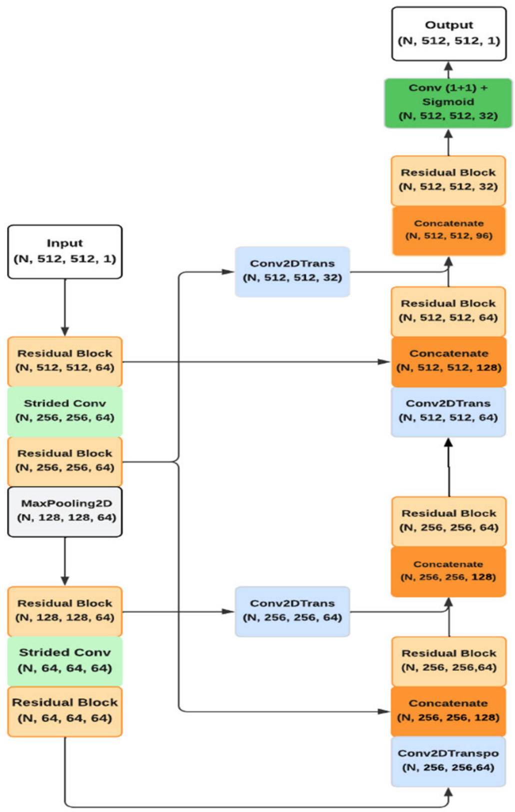

FIGURE 10. Number of filters of ColonSegNet V2.

characterizes the significantly higher computational complexity of the DL model. Unless properly addressed, these issues will have a negative impact on the deployment of automated AI-based eye disease diagnostics systems.

The contribution of our current work mainly focuses on reducing the computational complexity of the developed model (RV-SegNet) without compromising on its segmentation performance.

IV. METHOD

A. DETAILS OF THE BASIC MODEL ARCHITECTURE

We recently [29] developed an accurate and lightweight model for retinal vessel segmentation based on ColonSegNet [30]. ColonSegNet [30] is a real-time polyp segmentation Encoder-Decoder architecture. This architecture uses a residual block with a squeeze and excitation network. The architecture comprises two encoder blocks and two decoder blocks. Each encoder block consists of a 3×3 strided convolution between the residual blocks. Similarly, each decoder block contains transpose convolution and skip connections from the encoder block. The architecture of

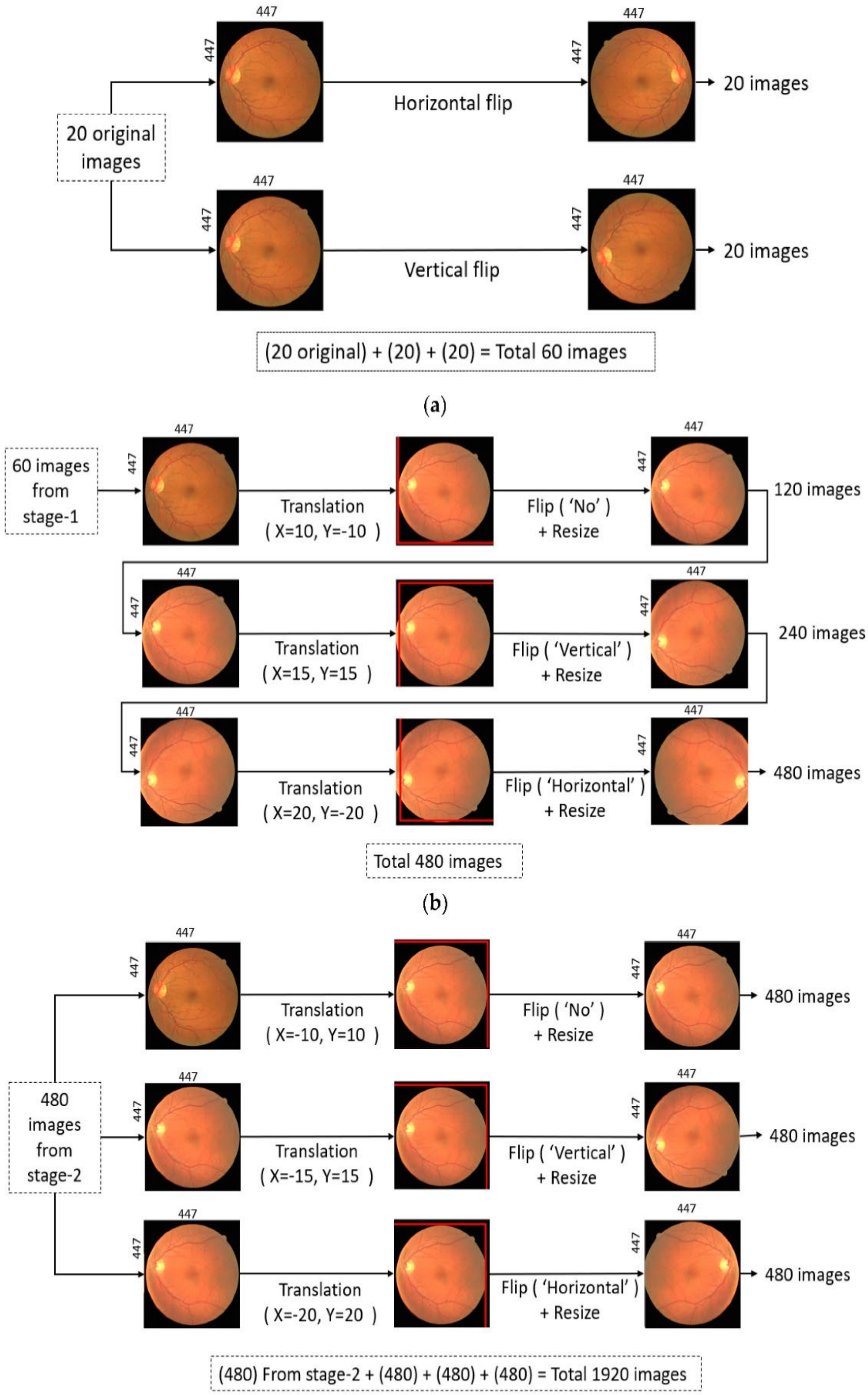

FIGURE 11. The various data augmentation strategies for generating a large number of images.

ColonSegNet [30] is depicted in the block diagram in Fig. 9. This model is advantageous due to its low computational complexity and a low number of trainable parameters, making it well-suited for low-end devices.

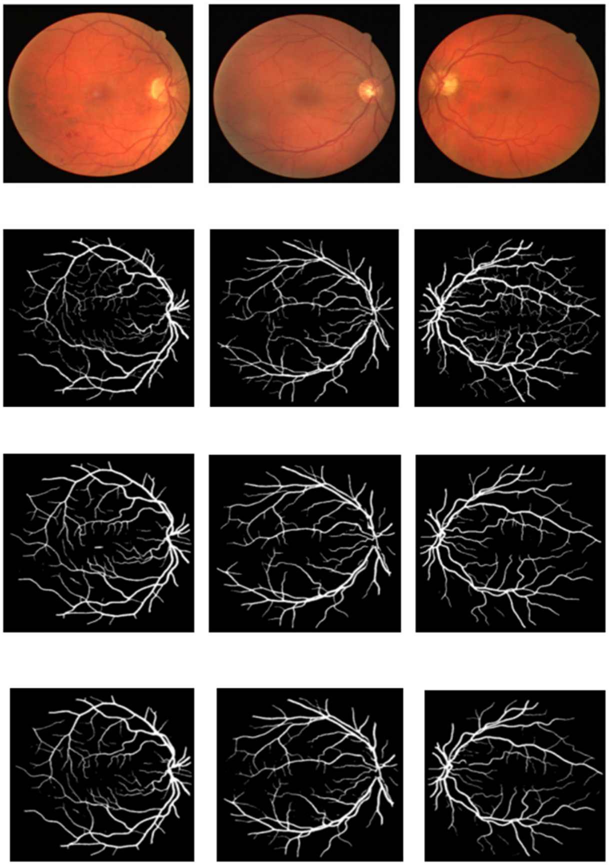

FIGURE 12. The qualitative performance comparison between colonSegNet [29] and RV-SegNet. First row presents three test images 2, 9, and 17 from DRIVE database. The second column indicates GT for all three samples. The third and fourth rows show the output of ColonSegNet [29] and ColonSegNet V2 respectively.

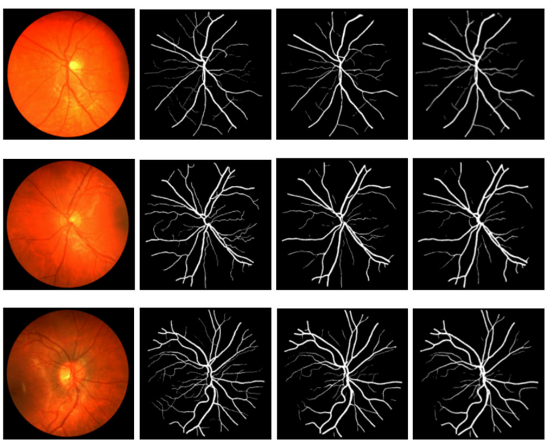

FIGURE 13. The analysis of vessels segmentation for image number 3, 4, and 5 from CHASE_DB1 dataset. The second column indicates GT for all three samples. The columns 3 and 4 indicate the output of ColonSegNet [29] and RV-SegNet.

B. DETAILS OF THE ENHANCED MODEL

This work aims to optimize an Encoder-Decoder-based architecture to reduce the computational complexity of the developed model without compromising on its segmentation performance. In the experiment, we examined how adjusting the number of convolution kernels impacted the model's standard evaluation metrics. It is important to mention that the number of filters can really affect how well the model performs and how many parameters it ends up with. This experiment aimed at reducing the computational complexity of the developed model (termed as RV-SegNet) while ensuring that its segmentation performance remains unaffected. As shown in Fig. 10, the number of filters was fixed by 64 filters in all blocks of the Encoder parts and the blocks of the first part of the Decoder. However, in all of the blocks in the second part of the Decoder, only 32 filters were used.

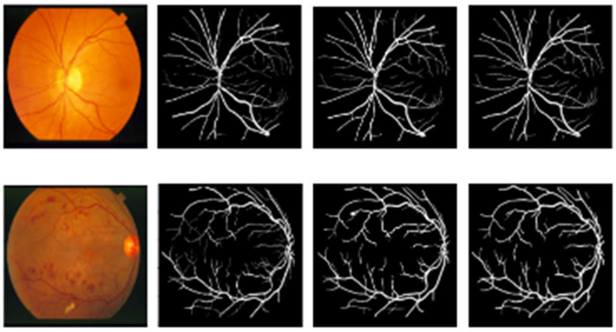

FIGURE 14. The analysis of vessels segmentation for image number im0163 and im0139 from the STARE dataset. The second column indicates GT for all three samples. The columns 3 and 4 indicate the output of ColonSegNet [29] and RV-SegNet.

V. RESULTS ANALYSIS

For the performance improvement of the DL model, one of the ideas is to explore the optimal values for clip limit and contextual region of CLAHE using intelligent evolution algorithms. After optimal contrast enhancement, it is recommended to apply some intelligent method for efficiently locating the optic cup and optic disk in the enhanced images using any of the suitable methods [31]. Both the contrast enhancement and cup/disk detection significantly improve the performance of the developed DL model. Numerous studies applied DL approaches for OD and OC segmentation in retinal fundus images [32], [33], [34].

It seems that the ColonSegNet V2 has been able to achieve a significant improvement in performance while still maintaining a lower level of computational complexity compared to other existing technologies. According to the proposed work, there has been a reduction in the number of parameters used from 5.00M to 982,177, compared with our recent work [29].

A. QUANTITATIVE PERFORMANCE COMPARISON

The performance of DL models for retinal vessel segmentation is summarized in Tab. 1 while the performance of DL models for OD and OC segmentation of numerous notable works on DRISHTI-GS and RIM-ONE databases is presented in Tab. 2 and Tab. 3 respectively.

Another challenging issue is the availability of fewer graded images in publicly available retinal image databases. Data augmentation is a generally applied solution for solving this problem. Generally, the researchers apply various kinds of data augmentation, for generating enough images for better training of their developed DL model. The data augmentation assists in overcoming the over-fitting issue in the training of the developed DL model.

The authors in [35], elaborated some techniques for artificially generating enough images using data augmentation techniques, which is required for optimal training of any developed DL model. They applied various data augmentation strategies on the twenty images and the corresponding gold standards of the DRIVE database. They graphically presented the various data augmentation steps including flipping (vertical/horizontal) and translation with crop-resize (nearest-neighbor interpolation), which we have shown in Fig. 11 [35].

They performed the data augmentation in three stages i.e. flipping, translation with recursive flip/resize, and translation without flip/resize. In the first stage of their data augmentation, they generated twenty images using the horizontal flip operation and additional twenty images using the vertical flip operation. So, the flipping operation produced 40 images shown in Fig. 11 (a). In the second stage of the data augmentation, the available 60 images were used for translation in both vertical and horizontal directions, in addition to flipping and resizing recursively, which produced 480 images as shown in Fig. 11 (b). In the final stage, the obtained 480 images were separately translated in both vertical and horizontal directions, in addition to flipping and resizing non-recursively, which produced $480 + 480 + 480 = 1440$ images shown in Fig. 11 (c).

Furthermore, it is highly recommended to perform rotation and mirroring for obtaining a sufficiently large database of images, which will help solve the class imbalance issue, in addition to solving the over-fitting issue of the DL model.

B. THE QUALITATIVE PERFORMANCE COMPARISON OF OUR PROPOSED MODEL

The qualitative performance comparison of our proposed model ColonSegNet V2 is shown in Fig. 12, Fig. 13, and Fig. 14. The first row in Fig. 12 presents three test images from the DRIVE database, 2, 9, and 17. The second column indicates GT for all three samples. The third and fourth rows show the output of our recent work [29] and RV-SegNet, respectively.

The first row in Fig. 13 presents Image numbers 3, 4, and 5 from the CHASE_DB1 dataset. The second column indicates GT for all three samples. Columns 3 and 4 indicate the output of our recent work [29] and RV-SegNet. Fig. 14 presents Image numbers im0163 and im0139 from the STARE dataset. The third and fourth rows show the output of our recent work [29] and RV-SegNet, respectively. From our observation of these results, we can say that the proposed model can detect the vessels better than [29].

VI. CONCLUDING REMARKS AND FUTURE DIRECTIONS

This work highlights the various challenges faced by researchers and developers in designing and developing automated systems for disease diagnosis, specifically for eye diseases. The limited number of images in publicly available retinal image databases leads to under-fitting and over-fitting issues of deep learning models. To overcome this, data augmentation procedures are recommended for generating a large number of images. Furthermore, pre-processing techniques such as contrast enhancement and noise removal are necessary before training/testing deep learning models. The trade-off between computational complexity and evaluation metrics should also be considered to enable deployment for large-scale population screening. Strategies and solutions for addressing challenges in retinal vessels and OD/OC segmentation are presented, which will assist in developing state-of-the-art deep-learning models for eye disease classification, including Glaucoma and Diabetic Retinopathy.

One limitation of this work is that the proposed deep learning models may struggle to accurately detect very thin vessels in retinal images, which can be a critical factor in the diagnosis of certain eye diseases.

Future research should focus on developing more advanced segmentation techniques that can effectively detect and segment these very thin vessels, potentially through the incorporation of additional features or information beyond what is currently used in the proposed models.

CONFLICTS OF INTEREST

The author declares that there are no conflicts of interest to report regarding the present study.

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