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Original Research Article

Application of Artificial Intelligence in the Management of Glaucoma and its Prognosis

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Abstract

Background: Glaucoma is a chronic progressive optic neuropathy characterized by damage to the optic nerve and visual field loss. About 2.1 million people were found to have blindness by developing Glaucoma worldwide. Glaucoma, after macular degeneration, is the second most common reason for irreversible blindness 2.93% of people aged 40-80 years have Glaucoma, among which many suffer open-angle Glaucoma. The evolution of Artificial Intelligence also revolutionized the examination and treatment processes. AI has suitably fit itself in this ophthalmic diagnosis. It is so because it highly magnifies even the deepest chambers of the optic region, thereby creating ease for ophthalmologists.

Aims: To analyze the efficacy of the selected programmed classifiers in the early detection of Glaucoma for proper diagnosis and management at the early stage for better prognosis.

Methods: A cross-sectional study was conducted on healthy and Glaucoma patients. All the patients underwent ophthalmic evaluation, and the tests were completed within six months. The study selected seven machine learning classifiers trained for early diagnosis of Glaucoma and to differentiate effectively from the normal eye. These classifiers were used appropriately in the early diagnosis of Glaucoma. The study statistically analyzed the outcomes generated by these classifiers.

Results: The study found an Area Under Curve (AUC) of 0.851, the worldwide vC/D, or vertical cup/disc ratio, was at best. The global GPS has the highest AUC of the seven GPS sectoral metrics (0.834). While not significantly better than global vC/D, RPART AUC in all 95 variables significantly improved over global GPS. Compared to both global vC/D & global GPS, SVM-radial, including all 95 parameters, showed a significant improvement.

Conclusion: The study concluded that these classifiers are significantly efficient in differentiating the glaucomatous eye from healthy ones at an early stage.

Keywords: Glaucoma, Classifiers, Artificial Intelligence, Eye, Photoreceptors.

Introduction

Glaucoma is a chronic progressive optic neuropathy characterized by damage to the optic nerve and visual field loss. It is typically associated with elevated intraocular pressure, leading to retinal ganglion cell degeneration. This condition can result in irreversible vision loss and is often accompanied by characteristic changes in the optic disc. Regular monitoring and treatment are necessary to manage the disease and preserve visual function [1]. In this, optic nerve degeneration, optic disc excavation, retinal ganglion cell loss, and retina nerve fibre starts thinning [2,3]. The ganglion cells in the retina are neurons of the CNS which take signals from photoreceptors and transmit them in axons via the optic nerve to the brain. High intraocular pressure with low perfusion and pressure in cerebrospinal fluid elevates the gradient in lamina cribrosa, causing papillary hypoperfusion., This develops structure changes and remodels lamina cribrosa for axonal transport in optic nerve fibres [4]. Anterior pores of lamina cribrosa elongates in open-angle glaucoma [5,6].

Structural change leads to different categories of Glaucoma. Chamber angle changes are visible in gonioscope-like protein or pigment deposition [7], causing pseudoexfoliation or pigment glaucoma [8]. About 2.1 million people were found to have blindness by developing Glaucoma worldwide [9]. Glaucoma, after macular degeneration, is the second most common reason for irreversible blindness [10] 2.93% of people of age 40-80 years have Glaucoma, among which many suffer from open-angle Glaucoma [11, 12]. Open-angle Glaucoma elevates with age [13, 14]. Ethnic African groups are more vulnerable to Glaucoma than Europeans [11]. Juvenile and congenital types of Glaucoma are rare [15].

High intraocular pressure is the leading risk identified for open-angle Glaucoma [16]. Ocular Hypertension Treatment Study revealed that lowering the increased intraocular pressure can decrease open-angle glaucoma risk to 4.4% from 9.5% [17]. Glaucoma has a negligible effect on sleep apnea, diabetes and hypertension [18-20]. Corneal configuration is also a structural risk factor in Glaucoma [21]. Firstly, a funduscopic examination retinal nerve and optic disc must be done. Tissue loss occurs at the neuroretinal rim, causing an enlargement in the optic nerve. [3-5]. Morphometric techniques are used to examine optical nerves [6] quantitatively. Optical coherence tomography is used to measure neuroretinal rim [7]. Newer imaging technologies enable accurate assessment of Glaucoma.

Intraocular pressure and corneal measurements are essential in the initial examination [22,23]. This measurement must be done often daily as intraocular pressure is prone to fluctuation. Glaucoma pathogenesis can be done by examining the chamber angle with a Gonioscopic examination. The visual field must be assessed for evaluating functional impairment, which occurs after loss in nerve fibres of the optic nerve [22]. The visual field varies with different levels of cooperation and concentration of patients. It created difficulty in defining the progress. Thus, the visual field must be examined a year after the onset of diagnosis [22] significantly.

Laser therapy is alternatively used when conventional local interventions cannot accurately lower the interocular pressure till the target range. However, Laser therapy accomplishes moderate lowering of high outflow of aqueous humour after laser trabeculoplasty [18] and lower production of aqueous humour after performing cyclophotocoagulation [28, 29].

Surgical interventions are accomplished when non-surgical treatment cannot lower the intraocular pressure until the target range. In contrast, non-surgical interventions cause intolerable side effects after some time. Glaucoma surgical interventions include categories like non-filtering, filtering and minimally invasive technique. Like, a stent is placed in the Schlemm canal in surgery of minimal invasion type [24]. It lowers outflow resistance with the help of trabecular meshwork, but this surgery only lowers the interocular pressure to moderate levels when performed with cataract surgery [25]. However, in recent years, the prevalence of surgical intervention has increased in diagnosing Glaucoma [26].

Moreover, the evolution of Artificial Intelligence also revolutionized the examination and treatment processes. AI has suitably fit itself in this ophthalmic diagnosis. It is so because it highly magnifies even the deepest chambers of the optic region, thereby creating ease for ophthalmologists [27].

In human history, Artificial Intelligence (AI) is regarded as the fourth industrial revolution [28]. Deep learning (DL) is a state-of-the-art technique of machine learning which imbibed substantial global interest in the past few years [29]. DL process input data by using a representation-learning methodology without any manual engineering. It projects on low-dimensioned images and recognizes intricate structures with high dimensions [29]. DL is used in ocular imaging, OCT, optical coherence tomography, and fundus photographs. Ophthalmic diseases like diabetic retinopathy (DR), [30, 31] glaucoma,[32] age-related macular degeneration (AMD)[33] and retinopathy of prematurity (ROP) [34] are assessed by DL.

Conventional methods of treating ophthalmic diseases include clinical examination with increased image-capturing devices. This system was expensive and time-consuming. AI is well suited for ophthalmological intervention. DL is best suited for these ophthalmic diseases and has its application in this field [35]. TDL application goes hand in hand with ophthalmic images like digital fundus photographs and visual fields. This technique is used in the diagnosis and screening of common vision-threatening diseases with highly accurate findings, such as diabetic retinopathy (DR) [36,37], Glaucoma, age-related macular degeneration (AMD), as well as premature retinopathy or ROP [38,39]. AI and DL are viable and valuable adjuncts for existing medical diagnosis and intervention. They are substituting as alternatives to human image graders and ophthalmologists.

AI gives a perfect blend and interaction to digital images and actual physical surroundings. It provides an accurate magnified view of even the tiniest space in the optic region [40]. AI is being increasingly used in ophthalmic surgeries. AR headsets improve ergonomics and visualization in the operating room, replacing traditional oculars in microscopes that caused ergonomic issues and extended duration problems for surgeons.

AI gives way to breakthroughs in automated screening for treating Glaucoma. It used both unsupervised and supervised ML. Earlier, while detecting glaucomatous colour fundus photos, Glaucoma was classified by segmenting optic cup and as per primitive feature extraction ways [41-43].

Artificial Intelligence (AI) enhances Glaucoma management by accurately analyzing extensive data, improving prognosis, and fostering patient-physician trust. AI's image-based assessment, utilizing iterative feature learning in hidden layers and analyzing image patches, addresses challenges in treating Glaucoma. It impacts management, screening, and remote monitoring, providing patients with better disease understanding. Approved AI algorithms are integrated into electronic medical records for enhanced outpatient management. The study aims to determine whether the selected classifiers can differentiate the condition of Glaucoma from the normal eye and to quantify and analyze the efficiency of the classifiers in early diagnosis of Glaucoma.

Materials and Methods

Subjects

A cross-sectional study was conducted on healthy and Glaucoma patients. All the patients underwent ophthalmic evaluation, and all the tests were completed within 11 months. A total of 50 patients were included in the study and divided into two groups healthy and glaucomatous eyes group, each with 25 patients. The patients were considered glaucomatous if they presented with glaucomatous VF loss and optic neuropathy. In glaucomatous optic neuropathy, there is >0.2 of inter-eye cup-disc ratio, thinning of the rims and focal notching, and the cup-disc proportion is more significant than 0.6, or peripheral haemorrhages. Suppose the hemifield test of Glaucoma is outside the normal limits. In that case, it is defined as glaucomatous VF loss, <5% of standard deviation, or depression of 3 or more non-edge points. If the patients presents with no history of Glaucoma, <21mm Hg of IOP, no signs of optic neuropathy, and the Hamprey pattern is seen outside the normal limits, then the patients are grouped as healthy eyes.

Machine classifiers

There were seven different machine learning classifiers trained: Generalized Additive Model (GAM), Recursive Partitioning and Regression Trees (RPART), a Generalized Linear Model to Gaussian Error (GLM-Gauss), a Linear Discriminant Analysis (LDA), a Support Vector Machine with just a linear kernel (SVM-linear), the Support Vector Machine with just a radial kernel (SVM-radial), as well as the Generalized Linear Model to Binomial Error (GLM-bin). There were classifiers implemented using SPSS software.

Akaike information criteria (AIC) were used to reverse selection in this group of 10 predictors. In addition to utilizing a machine classifier that extracts pertinent data, AIC was employed to reduce redundancies in the data and prevent overfitting. LDA divides people into Glaucoma- and healthy-affected groups according to a linear arrangement of the factors. It assumes that the data are separated and exhibit a Gaussian distribution into two classes by using limits for linear differentiation that maximizes variation between both courses while reducing variation inside types. After mapping the multidimensional variables into a feature space, SVM develops a hyperplane to divide healthy and glaucomatous eyes with the most significant possible distance between all instances and the hyperplane.

GAM presupposes that the expected severity of Glaucoma may be summarised as a smooth univariate function of the parameters. SVMs typically perform much better than other classifier types at recognizing more crucial factors and disregarding less crucial ones. GLM is a generalized variant of least-squares regression. A linear model only with given parameters can be used to depict the log of something like the probabilities ratio of a patient acquiring Glaucoma regarding health. The Gaussian, as well as binomial error models, were used to create GLMs. A decision-tree partitioning algorithm is RPART. The parameter space is divided recursively along individual parameters.

Inclusion and Exclusion Criteria

Patients who visit our hospital's outpatient clinic, adhere to the study protocol, and offer informed consent are included. Those who consent to participate in the study voluntarily do so.

If a patient's media opacity or inadequately dilating pupils interfere with fundus imaging or clinical vision, also if they regularly took medicines recognized to influence a thick retina, they have been disqualified from the study. Other ocular disorders outside Glaucoma were not taken into consideration. Also, patients were disqualified if they had underlying conditions that would impact the thickness of their retina or their visual field or if they had undergone eye surgery in the past that wasn't a successful cataract extraction.

Statistical analysis

cross-validation by eight and leave-one-out (LOO) studies were used to evaluate classifiers. The data set was divided into 8-folds with 25 pieces of data for each eightfold cross-validation. Eight distinct models were created for each classifier, with the classifiers being trained on seven folds and tested on the eighth. By pointwise averaging across folds, the specific area beneath the curve of the receiver is operational characteristics (AUC) for every categorizer was calculated. The DeLong method was used to compare the AUCs. Each classifier was trained using the whole data set, except one eye, before being tested on the remaining eye to determine Its accuracy. All eyes were selected as the test eyes after this was repeated. The precision is then determined by dividing the entire amount by observations by the number of correct predictions and 0.05 is the level of significance of alpha.

Ethical Approval

The authors gave the patients a full explanation of the study. The patient's consent has been obtained. The ethical committee of the involved hospital has approved the study's methodology.

Results

Table 1 shows the characteristics of the treatments. The patients were split into two teams, healthy eyes and glaucomatous eyes, with 25 patients in each group. Females are more in both groups. The mean age of patients is 42.9 and 63.1 in the healthy and glaucomatous groups, respectively. Caucasians are seen as high in number in both groups. The disc size is 1.82 mm^2 and 1.97 mm^2 in healthy and glaucomatous groups. The mean deviation of the visual field is -0.89 and -6.72 in the fit and glaucomatous groups, respectively.

Table 1: Baseline characteristics of the patients in each group of this study

Variables	Healthy eyes (n=25)	Glaucomatous eyes (n=25)	P-value
Male: female	8.17	12.13	0.043
Age (years)	42.9 (15.8)	63.1 (14.2)	<0.0001
Visual Field pattern	1.75 (0.89)	5.92 (4.32)	<0.0002
Disc size (mm2)	1.82 (0.51)	1.97 (0.61)	0.031
	(0.91 to 3.21)	(0.81 to 3.71)	
Prescriptive deviation (dB)	(0.95 to 6.87)	(1.12 to 13.81)	
The mean deviation of the visual field (dB)	-0.87 (1.71) (-7.09 to 1.73)	-6.72 (7.16) (-27.34 to 0.64)	<0.0001

Table 2 shows the results of Glaucoma based on the machine classifier. With an AUC of 0.851, the worldwide vC/D, or vertical cup/disc ratio, was at best (Table 4). The global GPS has the highest AUC of the seven GPS sectoral metrics (0.834). While not significantly better than global vC/D, RPART AUC in all 95 variables significantly improved over global GPS. Compared to both global vC/D & global GPS, SVM-radial, including all 95 parameters, showed a significant improvement. Except for the GLM-binomial with all parameters and all RPART to narrower data sets, all machine classifiers appeared to have an AUC equal or greater than global GPS, albeit the differences were not statistically significant in any other case. Across RPART within all parameters & SVM-radial considerably improved global GPS & vC/D accuracy.

Table 2: Results of glaucoma discrimination by machine classifier

			GLM-Binominal	GLM-Gaussian	C/D ratio	LDA	SVM-linear	GLM-gaussian (10)	GAM	LDA	GLM-Binomial (10)	SVM-radial	REPORT
AUC	AUC		0.778	0.832	0.851	0.832	0.865	0.879	0.872	0.879	0.882	0.909	0.903
	AUC SE		0.036	0.035	0.035	0.035	0.029	0.031	0.032	0.031	0.029	0.019	0.019
	Sensitivity at 80% specificity		0.634	0.771	0.775	0.0771	0.769	0.817	0.794	0.817	0.815	0.862	0.862
	Sensitivity at 95% specificity		0.489	0.482	0.612	0.482	0.629	0.639	0.582	0.639	0.623	0.655	0.551
	p-value	Classifier vs GPS	0.219	0.991	0.552	0.991	0.372	0.143	0.291	0.143	0.119	0.009	0.017
		Global vertically C/D ratio vs the classifier	0.092	0.573		0.573	0.721	0.082	0.498	0.082	0.17	0.021	0.082
Accuracy	Accuracy		0.789	0.789	0.794	0.781	0.832	0.792	0.792	0.792	0.787	0.855	0.881
	p-value	Classifier vs GPS	0.684	0.934	0.726	0.741	0.152	0.801	0.801	0.801	1.002	0.021	0.005
		Global vertically C/D ratio vs the classifier	0.945	0.869		0.491	0.264	1.009	1.009	1.009	0.731	0.042	0.004

RPART, Recursive Partitioning and Regression Trees; C/D, cup/disc; SE, standard error; SVM, Support Vector Machines; AUC, area underthe receiver operating characteristics curve; GAM, Generalised Additive Model; GLM, Generalised Linear Model.

The area under the curve for receiver operating characteristics is known as AUC. Standard error, cup/disc, with Recursive partitioning & regression trees, or RPART Global positioning system, generalized additive model, generalized linear model, and support vector machines are all abbreviations for the same thing.

Discussion

Global glaucoma prevalence for people between the age gap of 40–80 is 3.4%. By 2040, 112 million people will be affected by Glaucoma worldwide [45]. Patients and Clinicians have warmly welcomed evolutions in disease detection. The developments also modified progressive functional and structural damages and optimized treatment to curb visual disability and long-term prognosis.

Glaucoma is a disease in which excavation of the neuroretinal rim develops. It created cupping at the head of the optic nerve, better known as optic nerve head (ONH) cupping. As ONH fluctuates, no cup-to-disc ratio (CDR) detects pathological cupping [46]. Li *et al*. [47] and Ting *et al.* [48] have generated computer algorithms to detect Glaucoma and CDR. Investigators have used ML technology to detect damage in glaucomatous nerve fibre using wide-angle OCTs [49]. Dl is used in assessing structural damages in the optic nerve in Glaucoma.

Atrophy of axons of retinal ganglion cells is done within a confined space. Ophthalmologists rely on less precise psychophysical data to draw the disease's final consequences. These outputs provide reliable parameters and normative comparisons but need more detailed functional analysis. Elze *et al*. [50] then developed a computer program to study VF for drawing VF loss patterns. This was rendered useful in glaucoma detection [51]. Moreover, many other computer programs were developed to detect VF progression for pointwise analyses [52,53]. Yousefi *et al*. [54] had already created a machine learning-based algorithm for VF progression even before the conventional strategies.

Progression of Glaucoma is still inevitable [55-57], suggesting that diversified treatment regimens still need to be formed. Kazemian *et al.* [58] used forecasting VF data projects and tonometric trajectories for glaucoma detection-patients, who are newly Glaucoma diagnostic fear of blindness [59]. Thus, ML can be used for patients' medical history for early detection and future risks of invasive surgical interventions.

Many AI technologies have been used to improve ergonomics. Unlike other ophthalmic diseases, Glaucoma used consensus findings in its detection, like intraocular pressure, fundus photographs, OCT and ocular biomarkers [59]. Fundus photographs are necessary to assess the optic CDR for peripapillary [60]. ONH parameters cannot be easily analyzed as the optic nerves of different patients are different sizes and shapes. RNFL varies with varying refractive indices. Therefore, early detection of Glaucoma requires efficient AI-based mechanisms for glaucoma screening [58, 59].

AI can make tangible and immediate betterment in the accuracy of clinicians. Experienced Ophthalmologists have self-confidence in treating severe glaucoma patients with significant complications. However, it is very feasible to miss early detection of Glaucoma because Glaucoma shows no signs in its early stages. Low sensitivity and missed diagnosis occurred in many patients with early-stage Glaucoma. Therefore, the need to improve the methodologies of diagnosis arises. With artificial Intelligence, diagnostic sensitivity improved very prominently. AI-enhanced the overall sensitivity of ophthalmologists to treat glaucoma cases. False negatives and false positives were reduced significantly. This AI advancement saved the unnecessary wastage of medical resources and provided efficient treatment for managing Glaucoma.

AI has certain limitations also. It efficiently analyses optical cup, disc, and retinal nerve fibre layer defects (RNFLD). However, it does not give any promising analysis of peripapillary atrophy and haemorrhage. The final diagnosis lacked these factors, which used AI-based algorithms.

Moreover, resizing issue of the image occurred while using Deep learning technology and graphic computational power. The delicate and intricate detailing in retina fibres is partially lost in the fundus image. This affected segmentation accuracy in the detection of RNFLD. The difficulty arises in detecting the age or stage of Glaucoma, i.e. early, middle or late. Therefore, the invention is impeccable for this field. However, the specific effects of this AI model must be verified. AI has typically advanced glaucoma screening, allowing it to treat Glaucoma.

Conclusion

The study concluded that these classifiers are significantly efficient in differentiating the glaucomatous eye from healthy ones at an early stage. The study showed that machine classifiers can substantially increase the ability to diagnose the glaucomatous condition compared to today's methods to differentiate between single metrics. Regarding glaucoma discrimination, SVM-radial and RPART exhibited the most significant improvement regarding all parameters. Compared to current glaucoma treatment methods, different algorithms classifier of HRT3 data provide considerable progress in identification. With machine classifiers, the prognosis for Glaucoma would be significantly improved, improving the patient's treatment outcomes. The author suggests exploring additional classifiers and conducting similar studies on diverse populations for more effective conclusions. Including patients with different conditions would help determine the significance and efficiency of the classifiers. It is also important to evaluate the performance of these classifiers at different stages of Glaucoma. The study utilized machine learning classifiers to diagnose glaucomatous eyes and analyzed their efficiency. Early diagnosis of Glaucoma is crucial for better management and prognosis, impacting socio-economic factors globally.

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