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INCIDENCE AND UPDATES MANAGEMENT OF DIABETIC RETINOPATHY

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ABSTRACT

One of the biggest causes of vision loss in the globe is diabetic retinopathy (DR), a consequence of diabetes. Despite significant attempts to lower the prevalence of vision impairment, DR continues to grow. There is damage to the vascular endothelial cells as the first pathophysiology of DRcells and a decrease in pericytes. As a result of the hypoxic reactions that follow, vascular endothelialvascular endothelial growth factor (VEGF) The most effective treatment available right nowControlling blood sugar levels is the key to preventing diabetic retinopathy and diabetic macular edema (DME). Superior in every way Laser therapy, anti-VEGF therapy, steroid therapy, and vitrectomy are all necessary treatments in these situations. Photocoagulation of the retinal pigment epithelium There is strong evidence that non-proliferative diabetic retinopathy (NPDR) is a viable treatment option.results that can be used to keep DR from progressing further. Furthermore, laser therapy has proven to be effective.For example, grid and subthreshold diode laser micropulse photocoagulation (SDM) for DME has been used.reported. In cases of vitreous hemorrhage or tractional retinal detachment in PDR patients, vitrectomy has been undertaken. There has also been significant interest in the ability of anti-VEGF medication to slow the progression of PDR from DME patients. Even with these therapies, many individuals with DR are still at risk of losing their eyesight and developing potentially dangerous side effects.. In the most advanced stages of DR, laser photocoagulation and vitrectomy are effective treatments for preventing severe vision loss. Both approaches, however, have their limitations. Evidence from preclinical and clinical studies shows that targeting renin-angiotensin system inhibition, vascular endothelial growth factor, and renin-angiotensin system blockade can reduce cardiovascular disease risk.the growth hormone, corticosteroids and protein kinase C.DR may be treated with these methodsMethodsThe study between January 2017 and November 2020 total number of patients 2968, Retrospective three year analysis.ResultsIncidence of referable retinopathy was independently associated with known duration of diabetes, age at diagnosis, and use of insulin treatment. For participants needing insulin treatment with a duration of diabetes of 10 years or more, cumulative incidence of referable retinopathy at one and three years was 9.61 and 30.99 per 1000 people, respectively.

Keywords: diabetic retinopathy; diabetic macula edema; anti-VEGF therapy; vitrectomy; laserphotocoagulation. corticosteroids, protein kinase C,advanced glycation end-products, growth hormone

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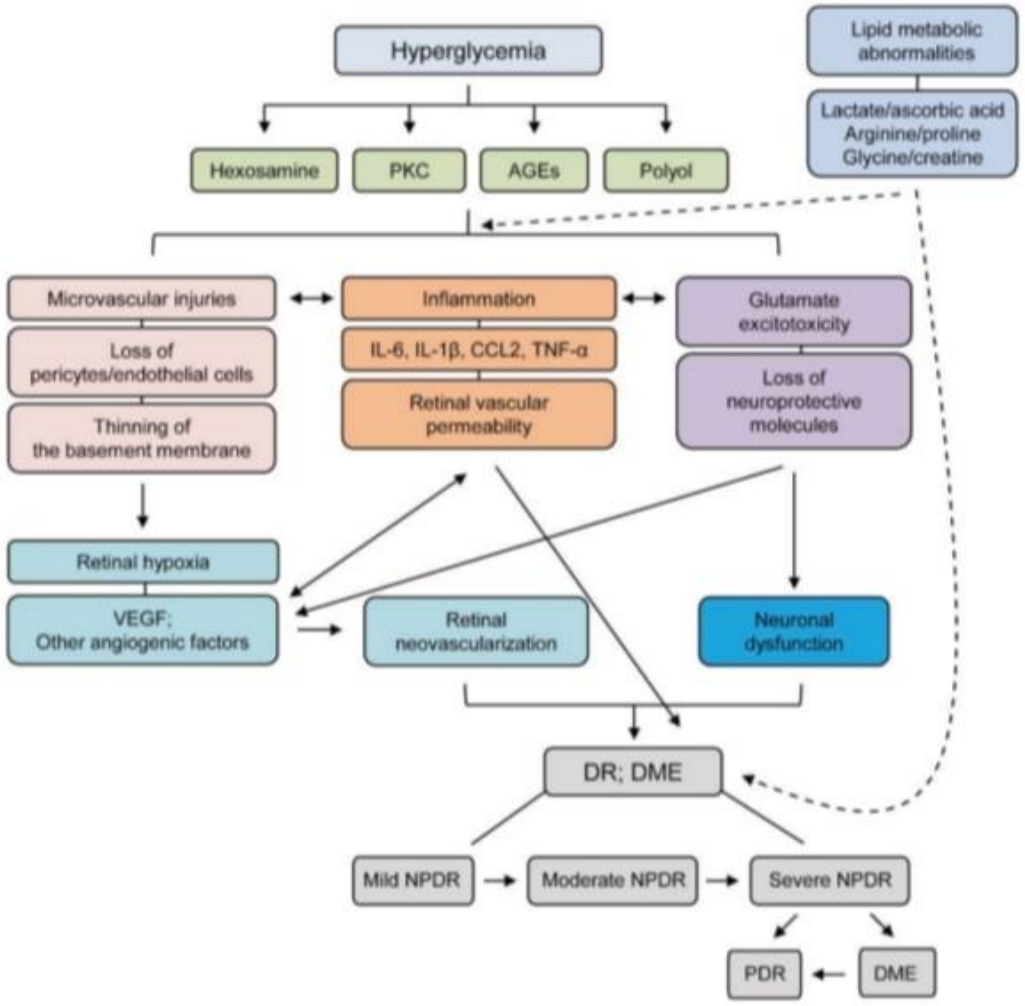
INTRODUCTION

As one of the most common causes of vision loss in people with diabetes, diabetic retinopathy is a serious side effect of the disease. The Vision Loss Expert Group (VLEG) found that DR was responsible for 1.25 percent of moderate to severe visual impairment and 1.07 percent of total blindness [1]. According to a meta-analysis, the percentage of DR-related blindness varies by geography, from 2 percent in Oceania and East and Southeast Asia to Southern Latin America has a population of 5.5 percent. Eastern and Western Europe and Southern Latin America were shown to have higher rates of DR-induced blindness than regions with younger populations [2]. Type 1 diabetes mellitus has a 42.1% DR rate, while type 2 diabetes mellitus has a 25.5% DR rate [3]. For patients with type 1 diabetes, the DR diagnosis was made in 32.58 percent of the time; for those with type 2 diabetes, the DR diagnosis was made in 23.14% of the time [4]. The Democratic Republic of the Congo has undergone a profound social and economic transformation .

There has been a rise in the expense of healthcare and an increase in its prevalence in the aging society. Since DR has a significant impact on public health, finding new and better treatments, such as laser, anti-vascular endothelial growth factor (VEGF) therapy, steroids, and vitrectomy, is critical [9]. In spite of advances in surgical and pharmacological treatment, the pathophysiology of degenerative disease is still unknown. Here, we examine the current putative pathophysiology of DR and the status of known surgical and/or pharmaceutical treatments.

Figure 1. A schematic illustration of the pathophysiology and stages of diabetic retinopathy (DR).



International Classification of Diabetic Retinopathy and disease severity

No Apparent DR — No abnormalities

Mild NPDR — Microaneurysms only

Moderate NPDR

More than just microaneurysms, but less than severe NPDR, (microaneurysms with other signs like intraretinal haemorrhages, hard exudates, cotton wool spots)

Severe NPDR

Any of the following: (4:2:1)

1. More than 20 intraretinal haemorrhages in each of 4 quadrants
2. Definite venous beading in 2+ quadrants
3. Prominent intraretinal microvascular abnormalities IRMA in 1+quadrant (And no signs of PDR)

PDR

One or more of the following:

1. Neovascularization
2. Vitreous/preretinal haemorrhage

Diabetic macular oedema (DME) by clinical appearance

No apparent DME --- No retinal thickening or hard exudates at the macula

Mild DME-

Some retinal thickening or hard exudates in posterior pole but distant from the centre of the macula

Moderate DME

Retinal thickening or hard exudates approaching the centre of the macula but not involving the centre

Severe DME

Retinal thickening or hard exudates involving the centre of the macula

DME classification by centre of macula involvement using optical coherence tomography (OCT)

Non-central involving DME

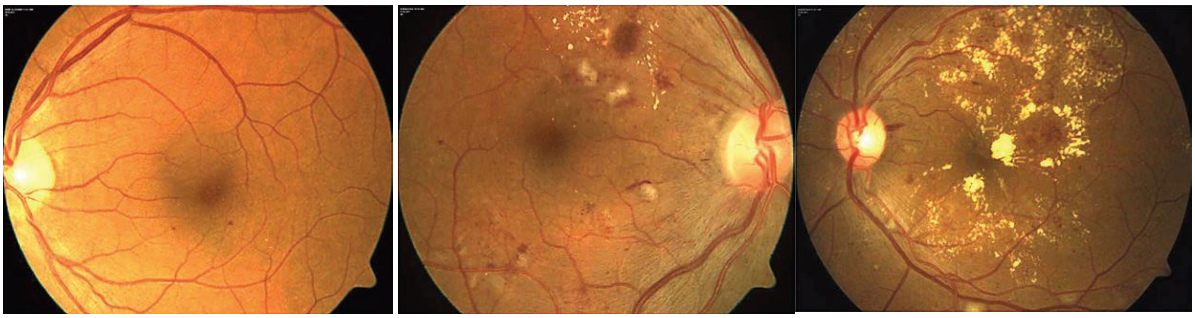
Retinal thickening in the macula that does not involve central sub- field zone in OCT (1 mm diameter)

Centre involving DME

Retina thickening in the macula that involves the central subfield zone in OCT (1 mm diameter).

Figure 2: *Clinical features of DR*

3.1. NPDR- Mild 3.2. NPDR- Moderate 3.3. NPDR- Severe



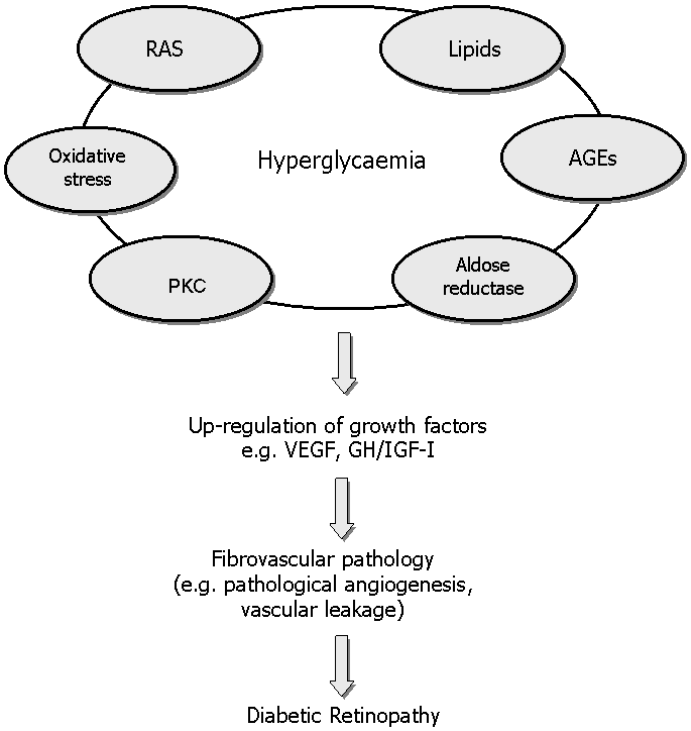


FIGURE 3. Schema summarising the factors involved in the pathogenesis of DR. RAS, renin-angiotensin system; AGEs, advanced glycation end-products; PKC, protein kinase C;VEGF, vascular endothelial growth factor; GH, growth hormone; IGF-I, insulin-like growth factor-I.

Diagnosis of DR

The diagnosis of DR is made from fundus examination, often aided by fundus fluorescein angiography (FFA), optical coherence tomography (OCT) and of late, optical coherence tomography-angiography (OCTA). The FFA is useful to qualify and quantify areas of capillary nonperfusion; the OCT is particularly useful to qualify and quantify macular oedema. The guidelines of the American

Academy of Ophthalmology for FFA and OCT are shown in Table 4 [13]. The South-East Asia diabetic retinopathy expert group agreed upon these criteria.

Table 1: *American Academy of Ophthalmology Guidelines for fluorescein angiography and optical coherence tomography .*

Investigation	Situation	Usually	Occasionally	Never
FFA	Investigate unexplained vision loss	X	-	-
	Guide laser treatment for DME	X	-	-
	Identify clinically suspect NVE/NVD	X	-	-
	Identify area of capillary non-perfusion	–	X	-
	Screen for DR	–	–	X
OCT	Investigate unexplained vision loss	X	–	–
	Identify areas of vitreo-macular traction	X	–	–
	Monitor response to treatment	X	–	–
	Evaluate patients difficult to examine	X	–	–
	Investigate other possible causes of macular oedema	–	X	–
	Screen for DR	–	–	X

Laser Treatment

A.Treatment for DR

The Diabetic Retinopathy Study (DRS) indicated four risk factors for vision loss in DR. These risk factors include the presence of vitreous or preretinal hemorrhage, the presence of new vessels, the location of new vessels on or near the optic disc, and finally, the severity of pathological conditions in new vessels [14]. According to this study, eyes with three or more risk factors are considered "at high risk" of vision loss in DR.

Laser treatment for DR has been well established for several decades. Since pan-retinal photocoagulation (PRP) can reduce retinal neovascularization, it has been performed to reduce the high-risk development of PDR [12]. An analysis using a rabbit model of retinal ischemia showed that photocoagulation suppressed ischemia-induced VEGF, vascular permeability, and angiogenesis promoted by VEGF [7].

B. Treatment for DME

The ETDRS showed that the focal/grid laser produced better outcomes than the natural course in patients with severe DME [9]. Severe macular edema is defined as retinal thickening that involves or threatens the macula's center. The focal/grid laser is recommended especially for DME that does not include the fovea and does not require frequent visits to the hospital for treatment. However, large or dense coagulation near the

macula may result in a paracentral dark spot. Furthermore, complications such as atrophic creep may occur in this chronic condition Based on these problems, the modified ETDRS laser was proposed in the Diabetic Retinopathy Clinical Research (DRCR) net in 2007 It is based on direct photocoagulation of capillary aneurysms with a minimally invasive setting and is becoming the standard. Recently, subthreshold diode laser micropulse photocoagulation (SDM), invisible retinal phototherapy, has been developed to treat DME

Anti-VEGF Treatment

A. Treatment for DR

Protocol S reported that anti-VEGF treatment (ranibizumab) resulted in significantly better visual acuity than PRP treatment for PDR patients [14]. In addition, the anti-VEGF group had substantially less peripheral visual field loss, faced fewer cases of DME, and a decreased need for vitrectomy compared to those in the PRP group. Other studies have also shown improvements in Diabetic Retinopathy Severity Scale (DRSS) scores as well as a lower risk of vitrectomy and DME with intravitreal anti-VEGF treatment (ranibizumab),
compared to PRP .

B. Treatment for DME

A multicenter randomized clinical trial showed that anti-VEGF drugs had a therapeutic effect for DME that involves the central macula [11]. The RESTORE study showed that ranibizumab and laser therapy improved visual acuity more than focal/grid laser in patients with DME . The RISE and RIDE study showed that ranibizumab improved visual acuity and macular edema in patients with DME. In terms of the efficacy of bevacizumab, ranibizumab, and aflibercept for DME, it is controversial in randomized clinical trials Anti-VEGF injection may increase the risk of high intraocular pressure, infectious endophthalmitis, and cataract, retinal damages.

Steroid Treatment

Steroid treatment is indicated when edema is diffuse throughout the macula. Steroids have an anti-inflammatory effect that helps to downregulate both pro-inflammatory and pro-angiogenic mediators, which are crucial for the development of DME.

Fenofibrate Therapy in DR

Fenofibrate is a well-known peroxisome proliferator-activated receptor alpha (PPAR_) agonist. PPAR_ is one of the members in the nuclear receptor family of ligand-activated transcription factors [13]. Heterodimerization of PPAR_ with the retinoic X receptor regulates the transcription of genes involved in cellular metabolism [13]. Fenofibrate could reduce free fatty acids levels by upregulating the synthesis of molecules for fatty acid transport and _-oxidation through the activation of PPAR_

Pemafibrate Therapy in DR

Pemafibrate is a new selective PPAR_ modulator, recently synthesized by Kowa Company, Ltd. as a more efficient and safer alternative to fenofibrate. Clinical studies in Japan demonstrated that pemafibrate showed superior effects on cellular metabolism compared to fenofibrate by improving liver function and increasing serum creatinine levels less likely or decreasing the estimated glomerular filtration rate.

Integration of Laser Therapy &Pharmacotherapy

In PDR, some reports have suggested that combination treatment with anti-VEGF and PRP may be superior to monotherapy in terms of NV regression and treatment burden. As indicated earlier, recent data from protocol S of the DRCR Network demonstrated that both PRP and intravitreal ranibizumab were similar in the prevention of severe visual loss and other complications in PDR suggesting that patient-specific factors such as compliance and financial impact be considered primarily in management decisions. deferredmacular laser was still required in over 30% of study eyes with center-involved DMEreceiving ranibizumab in the RISE and RIDE studies. Combination therapy with intravitreal corticosteroids has likewise yielded mixed results in terms of both VA stabilization or improvement and reduction in overall treatment burden

Surgical Management of Diabetic Retinopathy and Diabetic Macular
Edema

Currently, vitrectomy continues to play a critical role in the management of certain scenarios in DR. These include non-clearing vitreous hemorrhages, tractional retinal detachment in PDR, and vitreoretinal interface abnormalities impeding macular edema resolution. The exact role of vitrectomy in the management of DME, however, remains incompletely defined at presen.

METHODS

Study population

Every person known to have diabetes mellitus over the age of 18 years be referred to the Diabetic Retinopathy Screening Service for by their doctor, apart from those excluded on medical grounds (for example, those unable to attend screening owing to infirmity or comorbidity) or those already attending hospital based ophthalmology services because of retinopathy. Our four year retrospective analysis included data for all patients classified as having type 2 diabetes mellitus, diagnosed over the age of 30 years, and who attended screening between January 2017 and November 2020 total number of patients 2968

Screening procedure

A trained healthcare assistant assesses patients' current visual acuity in both eyes (achieved with or without glasses or with pinhole reading), using an illuminated 3 m Snellen chart. Tropicamide (1%) is then applied to each eye, and after about 15 minutes, a trained photographer takes two 45° digital retinal images per eye (one macular centred, and one nasal field) using a non-mydriatic Canon DGi camera (with
a 30D or 40D camera back). The retinal images are transferred to a central reading centre for grading. The photographers can also take additional images of the retina, lens, or iris if deemed necessary.
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Statistical analysis

We did statistical analyses using SPSS version 16 and Stata version 10; evidence of significance was taken as $P<0.05$ unless otherwise stated.

RESULTS

Table 1. Baseline characteristics of study participants

Participants without evidence of diabetic retinopathy at initial screening			
	Did not attend a further screening event	Attended at least one further screening event	
Characteristics	(n=1724)*	(n=1244)	P
Known duration of diabetes mellitus (years)	4.6 (4.8)	4.2 (4.4)	<0.001
Male	938 (55.0)	693(55.3)	0.087
Female	786 (46.0)	551 (44.2)	
Treatment withDiet	671 (38.9)	431 (34.6)	<0.001
Oral hypoglycaemic agents	946 (54.9)	721 (58.4)	<0.001
Insulin	107 (5.7)	92 (5.4)	<0.001

Group includes eligible participants only. †Mean (standard deviation). ‡Number (%).

Table 2 Yearly incidence of any and referable diabetic retinopathy in participants using insulin treatment and without retinopathy at baseline

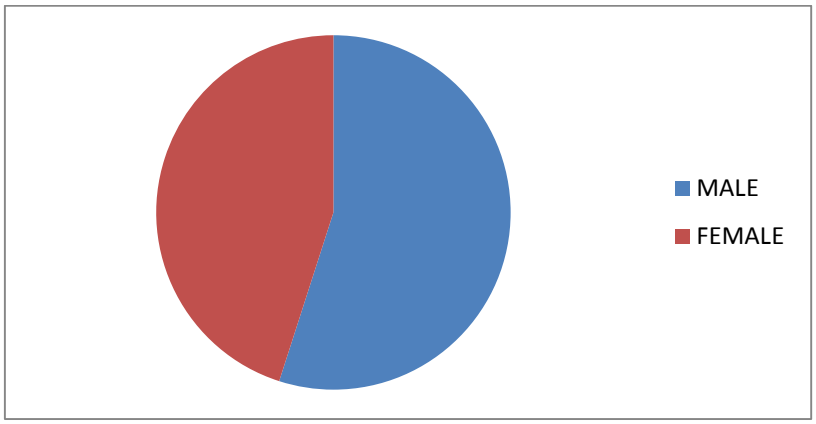
	Any retinopathy		Referable retinopathy	
Time from last negative Any retinopathy Referable retinopathy screen	Annual incidence	Cumulative incidence	Annual incidence	Cumulative incidence
1 year	31(12.1to 12.1)	31 (12.1 to 12.1)	2.01 (1.61 to 2.44)	2.01 (1.62 to 2.42)

2 years	22 (8.2 to 9.3)	54 (21 to 22)	2.81 (2.50 to 3.12)	4.81 (4.22to 5.43)
3 years	19 (7.3 to 7.5)	73(28.4 to 29.2)	3.23 (2.72 to 3.68)	8.05 (7.21 to 8.91)

Data are incidence (95% confidence interval) per 1000 people. Incidence of background retinopathy is the difference between the incidences of any and referable retinopathy.

Table .3.Summary of study

	NO.	%
Male	1631	
Female	1337	
Total	2968	
Laser Treatment	2077	70%
Anti-VEGF Treatment	1178	40%
Steroid Treatment	1929	65%
Fenofibrate	148	5%
Pemafibrate	118	4%
Integration of Laser Therapy & Pharmacotherapy	2671	90%
Surgical Management	415	14%



Figer 4 show male to femal ratio

Table 4 Complications linked to Diabetic Retinopathy

Specific	Non-Specific
Retinal Detachment Cataract	
Rubeosis Iridis	
Cataract	Glaucoma
Optic Neuropathy	Retinal Vein Occlusion/Optic Disc Swelling

DISCUSSION

Diabetes mellitus patients who had no evidence of diabetic retinopathy at baseline screening were shown to have a yearly incidence of any diabetic retinopathy in our study .One thousand patients each

year, 124.94 (12.5 percent) had retinopathy, which dropped to 66.59 (6.7 percent) in the third year of the study, At the end of three years, there were 360.27 cases per 1000 individuals (36.0 percent). Referable retinopathy had a low yearly incidence of 2.02 (0.2 percent) per 1000 participants in the first year, with a modest increase.

0.4) 3.54 percent) in the three years; the total incidence was 11.64 (1.2 percent). Referable retinopathy was shown to be inversely related to age at diagnosis and to be connected with both the known duration of disease and the necessity for insulin treatment. The cumulative incidence of referable diabetic retinopathy at one, two, and three years was 1.83, 3.66, and 5.45 per 1000 individuals for participants on diet treatment with diabetes for fewer than five years. Contrastingly, the equivalent figures for persons on insulin treatment for more than ten years were 9.61, 17.10, and 24.26 per 1000 people; this represents a roughly fivefold increase. Participants with diabetes for more than ten years who did not use insulin had values of 2.24, 5.86, and 10.33 per 1000, respectively .
Insulin-treated persons with diabetes for less than 10 years have rates of 0.71, 3.80, and 10.10 per 1000 people, respectively. People with diabetes mellitus may benefit from the findings .
A 12-month gap for screening could be used if no evidence of retinopathy was seen at screening, but this is unlikely. Diabetes patients who have been on insulin for at least ten years should be examined at least once per year going forward.

CONCLUSION

Diagnostic re-evaluation will be guided by new imaging techniques and the capacity to identify and quantify DR characteristics. When it comes to dealing with both DR and DME, ocular and systemic medication is the major mechanism of care. In DME, conventional laser therapy has evolved into a secondary intervention; it may also do so in PDR. Subthreshold laser treatment offers interesting properties, but further study is needed. What's still missing is the best way to combine these therapies . modalities. As always, the goal is to reduce clinical disease to the greatest extent possible in the shortest amount of time, with the fewest side effects, for the longest length of time, and at the lowest possible cost. In order to undertake clinical trials on hypothetical solutions, a big, independent consortium such as the NIH will be necessary .
The DRCR system. Regardless of the therapy chosen, any systemic comorbidities must be under control . is a significant factor in enhancing treatment outcomes. More research into this illness is needed, therefore we can only hope that in order to successfully treat DME and ultimately lessen its related consequences by discovering even better therapeutic methods.

RECOMMENDATIONS

Strict metabolic and blood pressure control, theexpert group recommended incrementally increasing care, as per the resource setting outlined earlier ,further studies in future.

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