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Progress in the Treatment of Retinal Vein Occlusion

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Abstract

Retinal vein occlusion (RVO) is a fundus retinal vascular disease under the combined action of local and systemic factors. Its etiology and pathogenesis are complex, and it is not completely clear. At present, there is no complete cure for this disease in clinical practice. The main treatment purpose is to control the progress of the disease and prevent the occurrence of serious complications (such as vitreous hemorrhage, neovascular glaucoma, etc.). This article reviews the progress in the treatment of RVO.

Keywords

Retinal Vein Occlusion, Macular Edema, Treatment

1. Introduction

RVO is a heterogeneous disease with an incidence rate second only to diabetic retinopathy in clinical settings. It usually involves damage to the venous return of the retinal circulation [1]. According to the location of the blockage, RVO can be classified as retinal branch vein occlusion (BRVO), hemi-retinal vein occlusion (HRVO), and central retinal vein occlusion (CRVO) [2], According to the severity of ischemia, RVO can be further classified into ischemic RVO and non-ischemic RVO [3]. Clinically, CRVO is less common than BRVO. Epidemiological studies have shown that the incidence of BRVO worldwide is approximately 0.4%, while the incidence of CRVO is about 0.08%. There is no significant difference between men and women. However, the risk of this disease increases with age. The cause of RVO is complex and is caused by local eye risk factors such as glaucoma and short eye axis, as well as systemic risk factors such as hypertension, diabetes, atherosclerotic diseases, hyperlipidemia, and abnormal coagulation function. The specific pathogenesis is not yet fully understood [4]-[6]. In patients with RVO,

macular edema (ME) is the most common cause of vision loss. Regardless of whether the macula (the central area of the eye where visual cells are densely distributed, located 0.35 cm posterior to the optic disc on the temporal side and slightly below it) is perfused or not, if the vision loss caused by angiogenesis is not effectively treated, the blood-retina barrier (BRB) will rupture or undergo permanent damage, leading to mild inflammation and relative ischemia, which may cause vitreous hemorrhage, tractional retinal detachment or neovascular glaucoma [7]. There are various treatment methods for RVO in clinical practice. However, there is no unified standard for the selection of treatment plans at present, and further discussion is needed. The main treatment options include: etiological treatment, drug therapy, surgical treatment, fundus retinal laser photocoagulation, and combined treatment, etc. This article provides a brief summary and classification of the treatment methods for RVO, aiming to offer certain references for future clinical research and treatment.

2. Etiological Treatment

In recent years, various risk factors related to the onset of RVO have been discovered, which make the systemic underlying diseases such as atherosclerosis, hypertension, hyperlipidemia, and hyperglycemia closely related to the occurrence of RVO, and all can increase the risk of its occurrence. Therefore, early detection, early diagnosis, and active treatment of the underlying diseases play a crucial preventive role in the occurrence and development of RVO.

3. Drug Treatment

3.1. Glucocorticoid

3.1.1. Triamcinolone Acetonide

Triamcinolone is a type of steroid hormone commonly used in ophthalmology for intraocular treatment. Its main purposes are to inhibit proliferation, reduce edema, and suppress the formation of new blood vessels. The therapeutic effect of triamcinolone on RVO is mainly achieved by reducing the permeability of retinal capillaries and inhibiting the expression of VEGF factors. The standard treatment for RVO compared with corticosteroid treatment (Standard Care vs. Corticosteroid for Retinal Vein Occlusion, SCORE) investigated the role of 1 mg or 4 mg of triamcinolone in the vitreous cavity and macular grid laser photocoagulation (GLP) in BRVO. The study included 411 BRVO patients and allowed re-treatment every 4 months according to the PRN standard. There was no statistically significant increase in visual acuity at the 12th month: the percentages of patients with an increase of 15 letters or more in visual acuity from baseline to the 12th month were 26.0% (1 mg), 27.0% (4 mg), and 29.0% (GLP), the average change in BCVA was 5.7 (1 mg), 4.0 (4 mg), and 4.2 (GLP), and the central foveal thickness of the macula measured by OCT decreased by 149 μm (1 mg), 170 μm (4 mg), and 224 μm (GLP) compared to the baseline. In the 4 mg triamcinolone group (41%), antihypertensive drugs were more common than the 1 mg triamcinolone group (7%)

and the GLP group (2%) within 12 months. 25% (1 mg), 35% (4 mg), and 13% (GLP) of patients experienced progression of cataracts [8]. The SCORE study also included 271 patients with CRVO who received intravitreal injections of 1 mg or 4 mg of triamcinolone acetonide for comparison. The same PRN standard allowed for re-treatment every 4 months. From baseline to the 12th month, the proportion of patients with an increase of ≥15 letters in BCVA was 26.5% (1 mg), 25.6% (4 mg), and 6.8% (observation), which was similar to the average loss of 12 letters in the observation group. The stable vision in the 1 mg and 4 mg triamcinolone acetonide groups was −1.2 and −1.2, respectively. The central point thickness measured by OCT was reduced by 196 μm (1 mg), 261 μm (4 mg), and 277 μm (observation) from the baseline. In the 4 mg triamcinolone acetonide treatment group (35%), the frequency of starting to use eye pressure-lowering drugs within 12 months was higher compared to the 1 mg triamcinolone acetonide treatment group (20%) and the observation group (8%), with 26% (1 mg), 33% (4 mg), and 18% (observation) of patients experiencing progression of cataracts [9]. Whether it is posterior vitreous injection or intravitreal injection of triamcinolone acetonide, both can alleviate macular edema in the short term and improve patients' vision. However, they may also aggravate the formation of cataracts, cause increased intraocular pressure, and lead to related complications such as endophthalmitis. Therefore, their use should be carefully considered based on the patient's condition.

3.1.2. Dexamethasone Implant

Ozurdex® (dexamethasone intravitreal implant) is a dexamethasone carrier developed in the form of a biodegradable intravitreal implant, which can deliver a 700μg dose of the drug to the retina and vitreous. It has been approved by the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the Swiss Medical Council for the treatment of ME associated with RVO [10] and non-infectious posterior uveitis [11]. Since inflammation is the key factor causing RVO-ME, Ozurdex® directly targets a series of inflammatory mediators. By inhibiting the proliferation and migration of various inflammatory cells and blocking the potential mechanisms of RVO-ME early on, it achieves protection of photoreceptor cells and effectively reduces macular edema. Ozurdex® can also be used in cases where the effect of anti-VEGF drugs has not been fully determined, namely ischemic retinopathy. There have been prospective studies proving its effective action for more than 12 months in ischemic RVO (although due to the ischemic state, the function is limited) [12] [13]. In the case of anti-VEGF treatment for retinal vascular diseases, the efficacy of dexamethasone implants in treating refractory macular edema has been proven [14]. For patients who have experienced cardiovascular events and are unable to tolerate monthly anti-VEGF drug treatment or follow-up, Aduris® can also be considered. Additionally, assessing the degree of ischemia in patients is a very important factor to consider. Not only the macular area should be focused on, but also the peripheral area. If macular edema is combined with ischemic factors, hormone combined with laser treat-

ment can be considered. The impact of Ozurdex® on the recovery of the retinal vascular barrier in patients with RVO is related to its effects on vision and central retinal thickness [15]. The main risk of complications from intravitreal dexamethasone implants is an increase in intraocular pressure, which reaches its peak 1 to 2 months after the first treatment. There have been no reports of an increase over time or with an increase in the number of injections. Monitoring and controlling intraocular pressure should be done within 4 weeks after implantation [16] [17]. At the same time, dexamethasone implants may also cause other complications such as cataracts and glaucoma. Although studies have confirmed that dexamethasone implants have a good therapeutic effect on RVO-ME and have a long-lasting effect in the vitreous cavity, which can significantly reduce the number of injections, due to the risks of these complications, further research is still needed for the use of dexamethasone implants.

3.2. Vitreous Cavity Drug Injection Procedure

At present, intravitreal injection of anti-VEGF drugs has become the preferred treatment method for RVO [18] [19].

3.2.1. Bevacizumab

Bevacizumab is a recombinant humanized monoclonal antibody targeting all subtypes of VEGF. Epstein *et al.* [20] evaluated the efficacy of intravitreal injection of Avastin in treating patients with CRVO-induced macular edema for more than 12 months. Sixty patients were assigned to receive intravitreal injection of Avastin or sham injection every 6 weeks for 6 months. All patients received intravitreal injection of Avastin every 6 weeks starting from the 6th month, and this continued for another 6 months. At the 12th month, the BCVA of the bz/bz group improved by 16.0 letters, while the sh/bz group improved by 4.6 letters. In the last follow-up, 18 out of 30 patients in the bz/bz group (60%) increased by 15 letters, and 10 out of 30 patients in the sh/bz group (33.3%) increased by 15 letters. The sh/bz group showed a reduction of 404 μm in CMT, while the bz/bz group had an average reduction of 435 μm in CMT. Intravitreal injection of Avastin can improve vision and alleviate macular edema. However, the visual improvement in patients receiving delayed treatment is limited. Other studies have also reported some side effects of Avastin's anti-VEGF treatment, such as damage to the macular microcirculation and retinal blood supply, and promotion of retinal vascular occlusion in RVO eyes [21]. Compared with ranibizumab, bevacizumab is less costly, but its overall therapeutic effect and safety are inferior to that of ranibizumab. Currently, the clinical application of intravitreal injection of bevacizumab is relatively rare.

3.2.2. Ranibizumab

Ranibizumab is a second-generation recombinant humanized monoclonal antibody Fab fragment with a relative molecular weight of 48,000. It can bind with high affinity to various isoforms of VEGF-A (VEGF165, VEGF121 and VEGF110) [22] [23]. The BRAVO study [24] (Evaluation of the efficacy and safety of ranibi-

zumab in treating macular edema caused by BRVO) enrolled 397 patients and randomly divided them into the Lucentis (0.3 mg) group, the Lucentis (0.5 mg) group, and the sham injection group. After 6 months, they were switched to the PRN regimen. At the 12th month, the percentages of patients in the Lucentis (0.3 mg) group, Lucentis (0.5 mg) group, and sham injection group who achieved a BCVA improvement of ≥ 15 letters were 56.0%, 60.3%, and 43.9%, respectively. The CMT reduction values were 313.6 μm, 347.4 μm, and 273.7 μm, respectively. Moreover, no new adverse events were found in this study. In the HORIZON trial, the open-label extension of the BRAVO study confirmed that the therapeutic benefits were typically maintained [25]. The CRUSE study [26] (Retinal vein occlusion (CRVO) with macular edema treated with ranibizumab: Efficacy and safety assessment) A total of 392 patients were included, who received monthly intravitreal injections of 0.3 mg or 0.5 mg ranibizumab or placebo for 6 months. Subsequently, PRN treatment with 0.3 mg or 0.5 mg ranibizumab and placebo was administered for 6 to 12 months. At 6 months, the average improvement in best corrected visual acuity (BCVA) score in the ranibizumab group was 12.7 (0.3 mg) and 14.9 (0.5 mg), while in the placebo group it was 0.8 letters; the proportion of patients with BCVA increase of ≥15 letters was 46.2% (0.3 mg), 47.7% (0.5 mg), and 16.9% (placebo); the average reduction in central foveal thickness (CMT) was 434 μm (0.3 mg), 452 μm (0.5 mg), and 168 μm (placebo). At 12 months, the average change in BCVA was 13.9 (0.3 mg), 13.9 (0.5 mg), and 7.3 (placebo/0.5 mg); the proportion of patients with BCVA increase of ≥15 letters at 12 months was 47.0% (0.3 mg), 50.8% (0.5 mg), and 33.1% (placebo/0.5 mg); CMT decreased to 452 μm (0.3 mg), 462 μm (0.5 mg), and 427 μm (placebo/0.5 mg), and no ocular adverse events occurred. This study confirmed the efficacy and safety of ranibizumab.

3.2.3. Conbercept

Conbercept is a new type of anti-VEGF drug. It is a fusion protein with a relative molecular weight of 143,000. Its composition structure consists of the immunoglobulin-like region 2 of human VEGFR1 (FLt-1) and the immunoglobulin-like regions 3 and 4 of VEGFR2, and fuses them with the Fc segment of human IgG1, making it have high affinity and a longer half-life. Studies have shown that the extracellular domain of VEGFR2 in Conbercept can significantly reduce the activity of new blood vessels, and at the same time enhance the binding of Conbercept to VEGF [27]-[29]. In the study by Huang YK *et al.* [30], compared with the normal control group matched by age and gender, the average BCVA, retinal vascular density and blood perfusion of 12 patients (12 eyes) with non-ischemic BRVO-ME were lower, while the CMT and the area of the foveal avascular zone (FAZ) were larger. These BRVO-ME patients received monthly intravitreal injections of Conbercept for 3 consecutive months. The results showed that after the injection of Conbercept, BCVA, retinal vascular density, blood perfusion increased, CMT significantly decreased, and macular edema was alleviated. This confirmed the definite efficacy of Conbercept in the treatment of non-ischemic

BRVO-ME. These results were consistent with most previous studies. Compassip has more binding sites, higher affinity, and even a longer half-life compared to monoclonal antibody anti-VEGF drugs [31] [32]. Therefore, it is questionable whether Conbercept causes more severe retinal vascular events than monoclonal antibody anti-VEGF drugs. In the study by Li FJ *et al.* [33], the treatment strategy for BRVO secondary to ME adopted a 1 + PRN approach. The results showed that BCVAs significantly improved ($p < 0.05$), and the average CMT significantly decreased ($p < 0.001$). At any follow-up time, there were no statistically significant differences in the improvement of BCVA, reduction of CMT, and injection frequency between the two groups. Therefore, the efficacy of conbercept and ranibizumab in treating BRVO secondary to ME was comparable. Additionally, during the follow-up period, no serious adverse events (systemic or focal) occurred in either group, such as stroke, arterial thrombosis, intraocular inflammation, cataract or lens damage, retinal detachment, retinal tear, or vitreous hemorrhage. The data indicate that intravitreal injection of conbercept for treating BRVO-ME is safe. Since conbercept has a stronger binding affinity to VEGFA than ranibizumab, it may be more effective in treating BRVO secondary to ME. Although the research data indicate that these two drugs have similar efficacy in treating BRVO secondary to ME, it is likely that the smaller molecular weight of ranibizumab enhances its penetration at the action site compared to conbercept, thereby offsetting its relatively lower binding affinity. Studies have shown that patients with RVO-ME who presented with serous macular edema characterized by retinal thickening before treatment, showed significant reduction in retinal thickness and improvement in macular edema after continuous injection of Conbercept for 3 months. No adverse reactions such as endophthalmitis or vitreous hemorrhage occurred. This proves the effectiveness and safety of Conbercept in the treatment of RVO [34]. In conclusion, intravitreal injection of Conbercept for the treatment of RVO is safe and effective.

3.2.4. Aflibercept

Aflibercept is a recombinant protein composed of two protein sequences of VEGF receptors (VEGFR-1 and VEGFR-2) and the Fc portion of immunoglobulin G1. The GALILEO study enrolled 177 patients with macular edema secondary to CRVO. They received 2 mg aflibercept intravitreal injection or placebo injection every 4 weeks for 20 weeks. The aflibercept group was treated with the aflibercept as-needed (PRN) regimen, while the placebo group continued to receive placebo injections for 24 to 48 weeks. At 6 months, the average increase in letters was 18.0 for the aflibercept group and 3.3 for the placebo group; 60.2% of the aflibercept group achieved ≥15 letters, while 22.1% of the placebo group did. The average CMT decreased by 448.6 μm in the aflibercept group and 169.3 μm in the placebo group [35]. At the 12th month, the patients in the aflibercept group increased by 16.9 letters, while those in the sham injection group increased by 3.8 letters. The average percentage of patients in the aflibercept group who gained ≥15 letters was 60.2%, and that in the sham injection group was 32.4%. Compared with the sham

injection group (−219.3 μm), the CMT in the aflibercept group (−423.5 μm) improved significantly [36]. From 12 to 18 months, the patients were monitored every 8 weeks. Both groups of patients received the Avastin PRN treatment regimen. During this period of 12 to 18 months, when the treatment interval was extended to 8 weeks, the visual and anatomical improvements were largely maintained [37]. No new adverse events were found during the follow-up period, confirming the safety and efficacy of Avastin treatment for RVO.

4. Surgical Treatment

4.1. Vitrectomy Surgery

The combined surgery of vitrectomy and internal limiting membrane peeling can relieve the traction of the vitreous on the retina in the macular area, improve oxygen supply, thereby reducing exudation and eliminating macular edema, achieving the goal of effective treatment for RVO. In the study by Park DH *et al.* [38]. 20 patients with CRVO and HRVO secondary macular edema underwent vitrectomy including internal limiting membrane peeling. The average follow-up was 61.2 months. Before the surgery, the average BCVA of 20 eyes was (1.50 ± 0.83), which improved to 1.06 ± 1.08 after the surgery. The follow-up after 60 months of vitrectomy ($p < 0.05$). At 60 months, the best corrected visual acuity improved by 0.2 log units or more in 13 out of 20 eyes (65%), 1 eye (5%) improved by 0.2 log units, 5 eyes (25%) remained unchanged, and 1 eye (5%) worsened. Mandelcorn and Nrusimhadevara reported [39] that in 8 eyes with macular edema caused by CRVO, 62.5% of the patients had improved vision after vitrectomy and internal limiting membrane peeling, and the macular edema was alleviated. The results of the above studies were better than the natural history data described in the Central Vena Cava Occlusion Study Group. Liang *et al.* [40] also reported that 75% of the 8 eyes with macular edema caused by CRVO had significant improvement in visual acuity. However, their average follow-up period was 14 months, and it could not show the effectiveness of the surgery anatomically. This surgery is difficult and risky, and has not been widely used in clinical treatment of RVO yet.

4.2. Laser-Induced Choroidal-Retinal Venous Anastomosis Surgery

Laser-induced chorioretinal venous anastomosis (L-CRA) refers to the process where, through the induction of laser, the obstructed veins, the Bruch membrane and the retinal pigment epithelium layer adjacent to the veins are simultaneously punctured, allowing the retinal veins in the fundus to be anastomosed with the choroid to form collateral circulation. This promotes the return of blood throughout the body, thereby improving the hypoxic state of the retina. In a randomized, controlled, multi-center, prospective clinical trial study [41]. The research results indicate that L-CRA has reasonable predictability. 76.4% of the patients achieved functional anastomosis, and surgical complications were effectively controlled.

For patients who actually had anastomosis, significant visual results were observed, and the rate of converting to retinal ischemia was lower than that of patients receiving standard treatment. The most important surgical complication of L-CRA surgery is the occurrence of new blood vessels at the anastomosis site. Currently, this surgical method is less used in clinical practice.

4.3. Surgical Incision of the Sheath at the Retinal Artery-Vein Crossing Point

BRVO refers to the obstruction of the branch veins of the retina. The obstruction mainly occurs at the intersection of the retinal arteries and veins. In theory, incising and reducing the sheath at this location can achieve the goal of improving blood circulation. The research results of Yamane S *et al.* showed that the arteriovenous sheath incision surgery significantly improved the BCVA of patients at 6 months and 12 months after the operation [42]. The results of a matched control study compared the effects of arteriovenous sheath incision surgery with that of observation alone and laser treatment in the matched control group. The results showed that the visual effect of the arteriovenous sheath incision surgery group was superior to that of the matched control group [43]. However, this surgical method has serious complications such as postoperative increase in intraocular pressure, retinal detachment, and rupture and bleeding of retinal blood vessels during the operation. Currently, this surgical method has been abandoned in clinical practice.

5. Fundus Retinal Laser Photocoagulation Surgery

Retinal laser photocoagulation is an important treatment method for RVO. It mainly involves using laser to promote the absorption of light energy by the retina and increase the blood flow in the retinal capillaries, thereby improving macular edema. At the same time, it reduces the permeability of the diseased blood vessels, decreases exudation, and can improve ischemia and prevent the formation of new blood vessels, thereby improving the patient's vision and further reducing the incidence of complications. The results of the Central Retinal Vein Occlusion Study (CVOS) indicate that laser did not show good efficacy in the trial population treated for macular edema caused by CRVO. However, a follow-up analysis revealed that the possibility of vision deterioration in the younger subgroup was reduced. Generally speaking, laser alone is not used to treat macular edema related to CRVO [2]. In the treatment of macular edema secondary to BRVO, the traditional methods of simple focal or grid laser photocoagulation have been replaced by intravitreal drug injections (IVI); however, if macular edema persists despite the use of existing intravitreal drugs, macular laser treatment can still be considered for BRVO patients. In these cases, central laser photocoagulation is based on the findings of fluorescein angiography, while diffuse pan-retinal laser photocoagulation is still applicable to RVO patients with large areas of hypoperfusion, the formation of new vessels, and/or advanced complications [44]. Laser treatment

may require frequent adjustments of laser intensity depending on the degree of retinal thickening and bleeding, and it may also cause complications. It is known that grid photocoagulation has potential side effects, including laser scar expansion, peripheral blind spot, increased central visual threshold, secondary choroidal neovascularization, subretinal fibrosis and outer retinal atrophy. These should be given sufficient attention. Recently, some researchers have recommended targeted laser photocoagulation in the peripheral non-perfusion area. It is expected that this treatment can not only improve the visual outcome of IVI therapy, but more importantly, it can also shorten the treatment time and the number of times of re-injection. In theory, if the ischemic retina around the eye leads to an increase in intraocular VEGF levels, then laser ablation of the affected retina can be used to block this source [2] [45]. However, conclusive evidence for targeted laser therapy does not yet exist. This is the focus of the ongoing prospective randomized controlled studies.

6. Combined Treatment

Although anti-VEGF drugs have shown good efficacy in treating RVO, their high injection frequency and high cost impose a heavy economic burden on patients. Currently, in China, the 3 + PRN treatment plan is the main approach. However, many patients are unable to continue the injections after the first injection, and repeated injections increase the occurrence of adverse reactions such as endophthalmitis and vitreous hemorrhage. This raises the question of whether multiple treatment regimens can be combined in clinical practice, and whether the combined treatment effect is superior to a single treatment regimen. In two case studies reporting the treatment with anti-VEGF and dexamethasone combination [46] [47]. In one of the retrospective interventional studies, 33 eyes of patients with RVO were injected with ranibizumab into the vitreous cavity, followed by dexamethasone injection, or only dexamethasone injection; the visual gain in the former group was more significant and faster than that in the latter group. In another prospective study, 34 eyes with RVO were intravenously injected with a combination of bevacizumab and dexamethasone, or only dexamethasone. The combined treatment regimen was proven to be more effective than the single treatment regimen, with greater visual improvement, significantly reduced retinal central thickness, and the visual gain persisted for a longer period. This also confirmed the results of the Shasta trial, in which if the combined anti-VEGF drugs were used with Ozurdex®, the duration of the combined treatment effect was prolonged, but the risk of increased intraocular pressure in the combined treatment group was higher. Azad S V found that the combined application of fundus retinal laser photocoagulation and anti-VEGF drugs could more significantly reduce the leakage of retinal vessels in the fundus retina, close the ischemic and hypoxic areas without perfusion, reduce the number of injections, and the overall treatment effect was better than the treatment with anti-VEGF drugs alone or fundus laser photocoagulation, which also better alleviated the economic burden of patients [48]. In addition, a

prospective, multicenter study found that the combined use of Ozurdex® and retinal laser photocoagulation can effectively treat macular edema caused by branch vein occlusion. The results showed that Ozurdex® and laser treatment work synergistically in improving the severity of macular edema, enhancing patient vision, and extending the injection interval [49] [50]. Combined therapy has opened up new possibilities for the management of RVO. However, it also brings new clinical challenges: the complexity of treatment plans, the long-term management of hormone-related side effects, the weighing of health economics costs, and the precise timing of combined treatment. In the future, with the widespread application of new generation long-acting drugs and the maturity of gene therapy technology, the treatment landscape for RVO will continue to evolve. But regardless of how technology progresses, the fundamental concept of combined therapy—addressing the complex pathways of diseases through multiple targets, multiple levels, and individualized approaches—will always run through clinical practice, becoming a profound and cautious art in the hands of ophthalmologists.

7. Concluding Remarks and Future Perspectives

Currently, intravitreal injection of anti-VEGF drugs is the first-line treatment for RVO in clinical practice. In both CRVO and BRVO conditions, the average level of VEGF in the vitreous will increase. However, in one-third of the eyes, despite the presence of ME, this level remains within the normal range [51]. This discovery indicates the existence of an independent VEGF-driven pathway that can drive ME, and this might be the reason why some patients have a poor response to anti-VEGF treatment alone. This might be a breakthrough to break through the treatment bottleneck. RVO is a chronic disease that seriously threatens patients' vision to a large extent. It is quite common in our daily life and is closely related to cardiovascular complications. Currently, there is no definite treatment method that can directly cure RVO in clinical practice. Instead, the current treatment strategies focus on minimizing the consequences of RVO, namely reducing macular edema and visual impairment caused by new blood vessels. Although anti-VEGF drug treatment is currently the standard for treating RVO, in some cases, laser and intravitreal steroid treatments are reasonable. The future treatment direction will focus on improving the current treatment plan. Recently, reports have shown that using robots for retinal central vein cannulation has been demonstrated, which may open the door to new strategies. Finally, the following persistent challenges should not be overlooked: the treatment bottlenecks for some patients with refractory RVO, the operability of long-term treatment follow-up, the medication compliance in real-world settings, as well as the prevention of neovascular complications in ischemic RVO, still require interdisciplinary integration and high-quality real-world research to be resolved.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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