

Original Article

Clinical benefits of laser therapy in von hippel-lindau syndrome: improved vision and reduced complications

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Abstract: Objective: To evaluate the long-term effectiveness of laser photocoagulation in treating retinal angiomas associated with von Hippel-Lindau (VHL) syndrome. Methods: A retrospective analysis was conducted on 80 patients treated at our institution for retinal angiomas due to VHL syndrome from January 2020 to January 2025. Patients were divided into two groups: the intervention group (n = 43) who received laser photocoagulation and the control group (n = 37) who underwent cryotherapy. Visual acuity, angioma characteristics, lesion reduction success, and other clinical parameters were assessed in both groups. Results: The laser-treated group demonstrated better visual outcomes than the control group, with significantly lower LogMAR values ($P < 0.001$). Additionally, fewer recurrences of retinal angiomas occurred in the laser-treated group, with a significantly longer time to recurrence compared to the control group ($P = 0.014$). The incidence of adverse ocular events, including retinal hemorrhage ($P < 0.001$), macular edema ($P < 0.001$), and visual field defects ($P < 0.001$), was significantly lower in the laser-treated group. Multivariate regression analysis further confirmed that laser photocoagulation ($B = 0.997$, $P < 0.001$) was a significant factor for long-term visual outcomes in patients with VHL syndrome, with an odds ratio (OR) of 0.369 (95% CI: 0.200-0.682). Conversely, the mean number of angiomas ($B = 2.079$, $P < 0.001$) was a significant factor, with an OR of 7.999 (95% CI: 4.397-14.550), indicating a strong correlation with poorer visual prognosis. Conclusion: Laser therapy photocoagulation improves visual outcomes and reduces the risk of complications and recurrence in patients with VHL syndrome. These clinical benefits are important for enhancing the quality of life in affected individuals.

Keywords: Long-term prognosis, laser treatment, retinal angiomas, von hippel-lindau syndrome

Introduction

Von Hippel-Lindau (VHL) syndrome is rare genetic disorder caused by mutations in the VHL gene, typically inherited in an autosomal dominant pattern [1]. It is manifested as a variety of vascular and tumor-related abnormalities, including retinal angiomas, hemangioblastomas in the brain, and pheochromocytomas. Retinal angiomas are the most common manifestation of VHL [2]. If left untreated, retinal angiomas can lead to complications such as hemorrhage, retinal detachment, and ultimately vision loss. With time, VHL can result in significant systemic disease burden, leading to severe, life-threatening consequences. The problems highlight the importance of effective

management strategies to preserve vision in affected individuals.

Retinal angiomas with VHL syndrome have been treated with cryotherapy [3]. Cryotherapy involves using a cold probe (cryoprobe) to apply extreme cold to the targeted tissue, causing necrosis of the abnormal blood vessels in the retina. While cryotherapy is a widely used technique for retinal conditions, it has limitations. One advantage of cryotherapy is its ability to treat multiple angiomas simultaneously, a benefit not always achievable with laser photocoagulation [4]. Nevertheless, cryotherapy carries significant risks, including scarring, vision loss due to retinal damage, and adverse events such as retinal hemorrhage and macular ede-

ma, which can exacerbate retinal disruption. Additionally, visual recovery after cryotherapy is generally slower compared to laser photocoagulation, making it less favorable for long-term outcomes.

Laser photocoagulation is commonly used in ophthalmology as the preferred treatment for retinal angiomas, particularly in patients with VHL syndrome. Its widespread use is largely due to its ability to preserve retinal health and control the progression of vascular damage [5, 6]. During laser therapy, the surgeon directs energy to the abnormal vessels, causing necrosis. Targeted closure of damaged vessels reduces the risk of serious complications, such as retinal hemorrhage, macular edema, and retinal detachment, which can occur if angiomas are left treated [7-9]. The initial outcomes are promising, as laser therapy successfully preserves eye health, maintains retinal function, and prevents further vision loss. However, despite the favorable short-term results, the long-term effectiveness of laser therapy, particularly in preventing recurrence and minimizing future complications, remains a subject of ongoing debate among experts.

This study investigated the long-term effects of laser photocoagulation in treating VHL-related retinal angiomas. Specifically, it will examine the effects of laser photocoagulation on visual outcomes, disease recurrence, and quality of life in patients. The goal is to provide valuable insights for clinicians in managing VHL syndrome and to improve patient outcomes. This research not only underscores the clinical relevance of laser therapy but also highlights its potential as an innovative method to managing a challenging and rare disease.

Methods

Case selection

This study retrospectively analyzed 80 patients with VHL syndrome-associated retinal angiomas, who were treated at Lishui People's Hospital between January 2020 and January 2025. Eligible patients were assigned into one of two groups: the intervention group (43 cases), which received laser photocoagulation for retinal angiomas, and the control group (37 cases), which received cryotherapy treatment. The study was conducted in accordance with the Declaration of Helsinki. Ethical approval

was obtained from the Lishui People's Hospital Ethics Committee.

Inclusion criteria: (1) Confirmed diagnosis of VHL syndrome, defined by either: a. A pathogenic VHL gene mutation, confirmed through genetic testing, or b. A clinical diagnosis based on family history and the presence of characteristic tumors, such as retinal angiomas, central nervous system hemangioblastomas, renal cell carcinoma, or pheochromocytoma [10]; (2) Confirmed diagnosis of retinal angiomas, as verified by fundus examination combined with imaging techniques, including fluorescein angiography and optical coherence tomography (OCT); (3) Laser photocoagulation as the primary treatment for retinal angiomas in the intervention group; (4) Regular follow-up and observation without active intervention in the control group.

Exclusion criteria: (1) Patients with incomplete or inadequate clinical data, which could not be used for outcome assessment or analysis; (2) Patients who underwent alternative treatment (e.g., other laser treatments, systemic medications, or surgical procedures) that could confound the study's outcomes; (3) Patients with severe comorbidity that could interfere with the treatment outcomes or impact the research results, such as uncontrolled hypertension or severe cardiovascular conditions; (4) Patients with severe conditions that could affect the study's findings.

Treatment method

In the intervention group, laser photocoagulation therapy was performed using a retinal laser photocoagulator (e.g. Carl Zeiss Visulas 532s) under local anesthesia. The laser was directly targeted at the retinal angiomas, with treatment settings tailored to each patient based on the size, location, and blood supply of the tumors. Argon laser coagulation, using a wavelength of 532 nm, was employed to prevent retinal hemorrhages, macular edema, and other complications. Some patients required repeated treatment sessions due to persistent angiomas. All patients were closely monitored for signs of recurrence, with regular follow-up visits for ongoing evaluation.

In the control group, patients received cryotherapy. A cryoprobe was employed to freeze the abnormal retinal vessels to induce tissue necrosis and vessel closure under local anes-

Table 1. Comparison of baseline characteristics between the two groups

Parameter	Intervention Group (n = 43)	Control Group (n = 37)	t/X ²	P-Value
Age (years)	34.21 ± 6.12	34.38 ± 5.41	1.070	0.288
Gender (Male)	22	19	0.001	0.987
Laterality of Retinal Angiomas	Bilateral: 28	Bilateral: 23	0.075	0.784
Mean Number of Angiomas	3.51 ± 1.22	3.84 ± 1.01	1.286	0.202
Duration of Follow-up (months)	36.58 ± 4.33	37.62 ± 3.85	1.127	0.263
Mean Visual Acuity (LogMAR)	0.34 ± 0.10	0.39 ± 0.17	1.626	0.108
History of Systemic Involvement	11	10	0.021	0.884

thesia. The freezing intensity was adjusted depending on the size and location of the angiomas. Cryotherapy aimed to halt further leakage and prevent additional retinal damage, with no significant complications reported during or after the procedure.

Outcome measurement

Electronic medical records were reviewed to gather data on patient characteristics, including the initial diagnosis, details of retinal angiomas (e.g., number, size, location), and any systemic manifestations of VHL syndrome.

The primary outcome was visual acuity, measured using the LogMAR scale at baseline and during follow-up visits. Visual outcomes at 36 months were categorized into three groups: improved, unchanged, and worsened.

Secondary outcomes included the occurrence of new retinal angiomas, progression of retinal vessels, and the number of complications. Changes in visual acuity were tracked throughout the 36-month period, and patients were classified based on improvements or deterioration in their vision. For assessing the laser treatment outcomes, macular visual testing and fluorescein angiography were conducted in both groups. Retinal angioma recurrence was monitored using OCT, WITH angiomas classified based on type and location (anterior or posterior). Other parameters such as the regularity of procedures, abnormal blood vessels growth, and the formation of new vessels were also noted. OCT measurements of retinal vessel thickness and occlusions were taken to track the progression of retinal vascular abnormalities, aiding in the evaluation of laser treatment efficacy in preventing major retinal issues. Quality of Life (QoL) was assessed on various domains, including vision-related quality of life, physical health, mental health, and daily func-

tioning. Scores were reviewed to assess the overall effects of laser therapy on health and well-being. Outcome measures were reviewed at baseline and at 3, 6, and 12 months, with follow-up assessments conducted 12 months later.

Statistical methods

Data analysis was conducted using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies or percentages and analyzed using chi-square tests. Continuous variables were expressed as mean ± standard deviation (SD) and analyzed using independent samples t-tests or repeated measures analysis of variance (ANOVA) followed by Bonferroni post-hoc tests. The association between the various factors (e.g., treatment type, number of angiomas) and visual acuity was assessed using a multivariate logistic regression analysis, with potential confounders adjusted for in the outcome measure. Statistical significance was set at a P-value of < 0.05 for all tests.

Results

Baseline characteristics

There were no significant differences in age (P = 0.288), gender distribution (P = 0.987), laterality of retinal angiomas (P = 0.784), or the number of cutaneous angiomas (P = 0.202) between the intervention and control groups (**Table 1**), indicating the comparability between the two groups.

Visual acuity outcomes

At baseline, both groups had similar LogMAR scores (P = 0.710). However, by 36 months, a significant difference in visual improvement was observed between the intervention group and the control group (P < 0.001). A greater

Table 2. Comparison of visual acuity outcomes between the two groups

Parameter	Intervention Group (n = 43)	Control Group (n = 37)	t/X ²	P-Value	Post-hoc Test
Baseline Visual Acuity (LogMAR)	0.37 ± 0.07	0.37 ± 0.07	0.373	0.710	0.710
Mean Change in Visual Acuity (LogMAR)	0.20 ± 0.05	0.32 ± 0.11	6.144	< 0.001	< 0.001
Percentage of Patients with Improved Visual Acuity	26	11	7.557	0.006	< 0.001
Percentage of Patients with Stable Visual Acuity	13	20	4.657	0.031	0.031
Percentage of Patients with Deteriorated Visual Acuity	4	14	9.287	0.002	< 0.001
Mean LogMAR at 36-month Follow-up	0.15 ± 0.04	0.36 ± 0.08	14.755	< 0.001	< 0.001

Table 3. Comparison of retinal angioma recurrence between the two groups

	Intervention Group (n = 43)	Control Group (n = 37)	t/X ²	P-Value
Overall Recurrence Rate	4	16	12.219	< 0.001
Time to Recurrence (Months)	26.33 ± 7.12	17.43 ± 3.20	7.005	< 0.001
Recurrence Rate by Angioma Location			1.686	0.194
Anterior	17	20		
Posterior	26	17		
Recurrence Rate by Number of Angiomas at Baseline			6.490	0.011
Fewer Angiomas	2	9		
More Angiomas	41	28		
Need for Retreatment	3	9	4.694	0.030
Impact on Visual Acuity (LogMAR)			6.491	0.039
Worsened	2	9		
Improved	3	2		
Stable	38	26		

proportion of patients in the intervention group experienced visual improvement compared to the control group ($P < 0.001$), while visual deterioration was less common in the intervention group ($P < 0.001$). At the 36-month follow-up, the mean difference in LogMAR scores between the two groups remained statistically significant ($P < 0.001$) (**Table 2**). Overall, most patients in the intervention group either improved or maintained their vision, suggesting the long-term effectiveness of laser therapy.

Recurrence of retinal angiomas

The time to recurrence was significantly longer in the intervention group (26.33 ± 7.12 months) compared to the control group (17.43 ± 3.20 months, $P < 0.001$). At the 36-month follow-up, recurrence was significantly lower in the intervention group (4 patients) compared to the control group (16 patients, $P < 0.001$). There was no significant difference in the location of angiomas between the two groups ($P = 0.194$), although the intervention group had a higher

proportion of posterior angiomas that did not recur (26 vs. 17). Patients in the intervention group with fewer baseline angiomas (2 patients) had a lower recurrence rate than those in the control group with fewer angiomas (9 patients, $P = 0.011$). Among patients with multiple baseline angiomas, recurrence was also significantly less frequent in the intervention group (41 patients) compared to the control group (28 patients, $P = 0.030$). The retreatment rate was significantly lower in the intervention group than in the control group ($P = 0.039$). Additionally, most patients in the intervention group maintained stable visual acuity (38 patients), whereas the control group showed more frequent changes in visual acuity ($P = 0.009$) (**Table 3**).

Adverse effects and complications

Results from the comparison of safety outcomes indicated that laser treatment was associated with fewer adverse effects. Adverse effects occurred significantly less frequently in

Table 4. Comparison of adverse effects and complications between the two groups

	Intervention Group (n = 43)	Control Group (n = 37)	χ^2	P-Value
Overall Incidence of Adverse Effects	9	16	4.609	0.032
Retinal Hemorrhage	2	11	9.191	0.002
Macular Edema	1	7	6.084	0.014
Retinal Detachment	3	9	4.694	0.030
Vision Loss	2	7	4.055	0.044
Need for Additional Interventions	4	8	2.367	0.124
Incidence of Post-Treatment Inflammation	11	2	5.127	0.024
Temporary Visual Disturbances	4	13	7.931	0.005

Table 5. Comparison of ocular function stability between the two groups

Parameter	Intervention Group (n = 43)	Control Group (n = 37)	t/ χ^2	Statistical Significance (p-value)
Stable Ocular Function	37	20	9.937	0.002
Ocular Pressure (mmHg)	16.07 ± 1.86	16.35 ± 2.86	0.529	0.598
Incidence of Glaucoma	2	5	1.956	0.162
Macular Function Stability	40	27	5.875	0.015
Retinal Sensitivity (dB)	30.35 ± 5.64	24.68 ± 4.56	4.899	< 0.001
Visual Field Defects	6	18	11.400	0.001
Progression of Retinal Vascular Abnormalities	5	14	7.544	0.006
Incidence of Retinal Inflammation	4	9	3.298	0.069
Mean Ocular Surgery Requirement (events)	0.14 ± 0.01	0.32 ± 0.02	44.586	< 0.001
Follow-up Duration (years)	5.86 ± 0.41	5.92 ± 0.28	0.731	0.467

the intervention group than in the control group ($P = 0.032$). In particular, the occurrence of retinal hemorrhage ($P = 0.002$) and macular edema ($P = 0.014$), both of which can cause vision loss, was much lower in the laser-treated group. Additionally, patients in the intervention group were less likely to experience temporary visual disturbances compared to those in the control group ($P = 0.005$) (**Table 4**). Overall, these findings suggest that laser treatment not only reduces the risk of serious complications but also promotes better visual outcomes with fewer side effects compared to observation alone.

Ocular function stability

A significantly higher proportion of patients in the intervention group maintained stable ocular function compared to the control group ($P = 0.002$). While the incidence of glaucoma was lower in the intervention group, this difference was not statistically significant ($P = 0.162$). Macular function stability was signifi-

cantly greater in the intervention group ($P = 0.015$), suggesting that laser treatment for retinal angiomas is more effective in preserving macular function. Additionally, retinal sensitivity was higher in the intervention group ($P < 0.001$), reflecting better retinal health. Visual field defects were less frequent in the intervention group than in the control group ($P = 0.001$). The progression of retinal vascular abnormalities was slower in the intervention group ($P = 0.006$), highlighting the positive impact of laser treatment in stabilizing retinal vascular changes. The incidence of retinal inflammation was lower in the intervention group, though the difference was not statistically significant ($P = 0.069$). The requirement for ocular surgery was significantly lower in the intervention group ($P < 0.001$), further indicating the effectiveness of laser treatment in reducing the need for additional interventions. Overall, the intervention group demonstrated superior ocular function stability, with fewer complications and better retinal health outcomes than the control group (**Table 5**).

Table 6. Comparison of long-term visual outcomes between the two groups

Parameter	Intervention Group (n = 43)	Control Group (n = 37)	t/X ²	Statistical Significance (p-value)
Mean Visual Acuity (LogMAR)	0.5 ± 0.11	0.51 ± 0.11	6.630	< 0.001
Visual Acuity Improved	26	1	7.557	0.006
Visual Acuity Stabilized	13	18	2.842	0.092
Visual Acuity Deteriorated	3	14	11.319	0.001
Incidence of Macular Edema	5	16	10.268	0.001
Central Retinal Artery Occlusion	0	4	4.893	0.027
Hemorrhage Frequency (mean events)	0.33 ± 0.10	0.51 ± 0.16	6.233	< 0.001
Retinal Detachment	1	8	7.416	0.006
Mean Follow-up Duration (years)	5.89 ± 1.95	5.44 ± 1.31	1.186	0.239
Changes in Retinal Vessels (mm)	0.21 ± 0.03	0.31 ± 0.02	16.428	< 0.001

Long-term visual outcomes

The intervention group demonstrated significantly better mean visual acuity compared to the control group ($P < 0.001$). A higher proportion of patients in the intervention group experienced improvement in visual acuity, while fewer experienced a decline, both with statistically significant differences ($P = 0.006$ and $P = 0.001$, respectively). The incidences of macular edema ($P = 0.001$), central retinal artery occlusion ($P = 0.027$), retinal detachment ($P = 0.239$), and hemorrhages ($P < 0.001$) were significantly lower in the intervention group compared to the control group. The duration of follow-up was similar between the two groups ($P = 0.239$). The details are shown in **Table 6**.

Quality of life

The quality-of-life scores, encompassing domains of vision-related quality of life score, physical health score, psychological health score, daily activity performance, and visual satisfaction were all significantly higher in the intervention group compared with the control group ($P < 0.001$, **Figure 1A-E**). Consequently, regarding overall quality of life, the intervention group demonstrated significantly better quality of life compared to the control group ($P < 0.001$, **Figure 1F**).

Need for repeated interventions

At the 36-month follow-up, the intervention group demonstrated a significantly lower rate of retreatment ($P = 0.030$) and longer time to retreatment ($P = 0.014$) compared to the control group. The average number of retreatments

required was also significantly lower in the intervention group ($P = 0.001$).

When specifically analyzing the need for retreatment due to retinal hemorrhage, the intervention group had a significantly lower rate compared to the control group ($P = 0.017$). Although the retreatment rate for new angiomas was also lower in the intervention group, this difference was not statistically significant ($P = 0.162$) (**Table 7**). These findings indicate that laser treatment not only reduces the need for repeated interventions but also significantly delays the occurrence of complications, such as hemorrhages and new angiomas, leading to better long-term management of retinal angiomas in VHL syndrome.

Correlation between baseline angioma characteristics and long-term outcomes

In the intervention group, patients with fewer baseline angiomas had a significantly lower recurrence rate compared to those with more angiomas, indicating that a higher baseline number of angiomas was associated with poorer long-term outcomes ($P = 0.028$). Similarly, in the control group, the recurrence rate was significantly lower for patients with fewer angiomas compared to those with more angiomas ($P = 0.024$). For posterior angiomas, the recurrence rate between the two groups was not significantly different, although the intervention group showed slightly better control ($P = 0.877$) (**Table 8**). These findings highlight the importance of baseline angioma characteristics in predicting recurrence risk and evaluating the effectiveness of laser treatment.

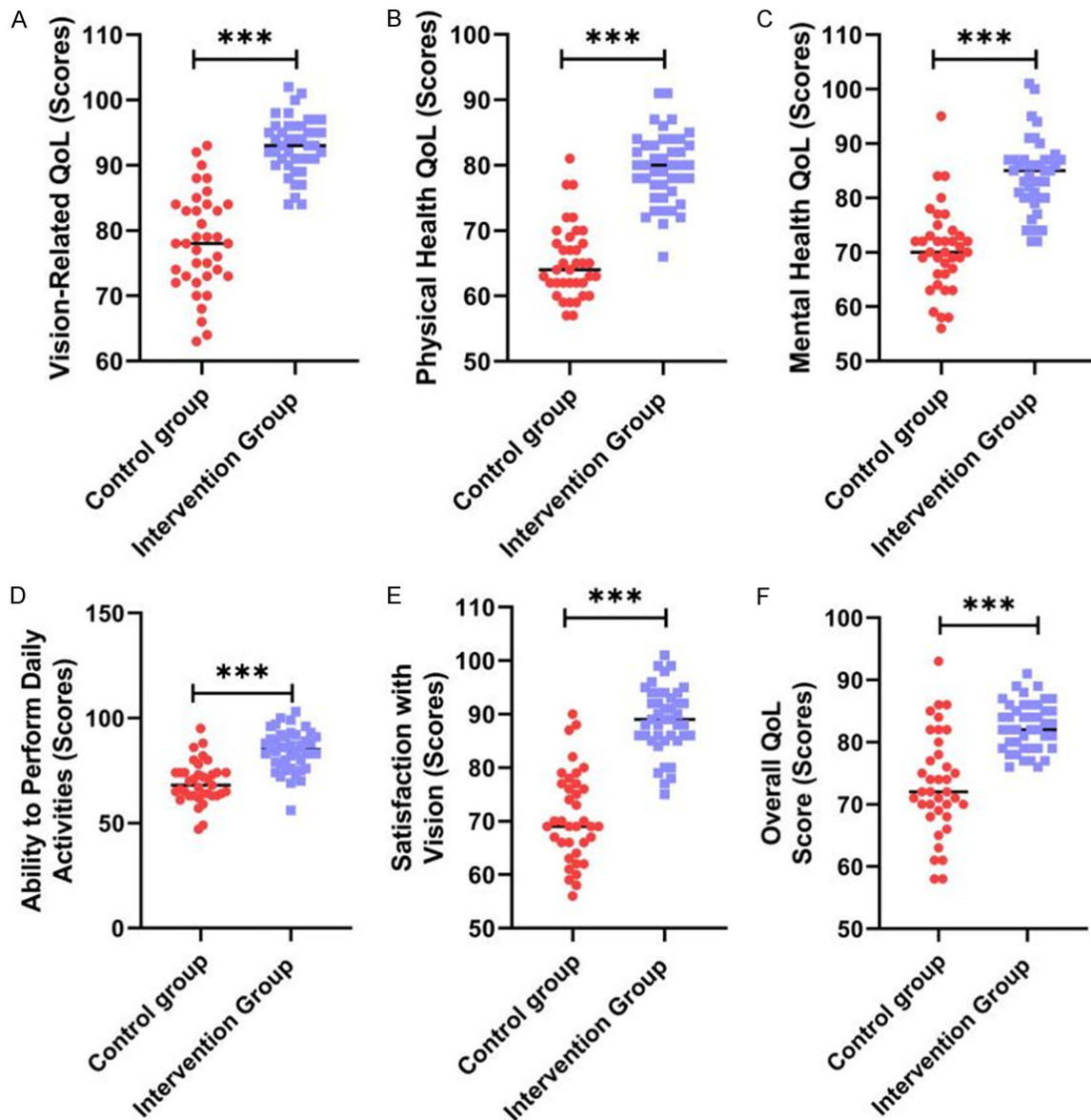


Figure 1. Comparison of quality-of-life (QoL) scores between the two groups. A. Vision-Related QoL; B. Physical Health QoL; C. Mental Health QoL; D. Ability to Perform Daily Activities; E. Satisfaction with Vision; F. Overall QoL Score. ***P < 0.001, compare with the control group.

Impact of laser treatment on the progression of retinal vascular abnormalities

The annual average progression rate of retinal vessels in the intervention group was significantly lower than in the control group ($P < 0.001$). Additionally, the incidence of retinal vascular abnormalities was significantly lower in the intervention group compared to the control group ($P < 0.001$). Regarding vessel diameter, the intervention group showed a significantly smaller increase compared to the control group ($P < 0.001$), indicating better control

of retinal vascular pathology. Regarding retinal neovascularization, the incidence was significantly lower in the intervention group ($P = 0.027$), suggesting that laser treatment effectively suppresses neovascular formation, which is a key factor in the progression of retinal diseases (Table 9).

Multivariate regression analysis of influencing factors for visual acuity

A multivariate regression analysis was performed to assess the factors influencing visual

Table 7. Comparison of the need for repeated interventions between the two groups

Parameter	Intervention Group (n = 43)	Control Group (n = 37)	t/X ²	Statistical Significance (p-value)
Need for Retreatment	3	9	4.694	0.030
Average Number of Retreatments	0.21 ± 0.04	0.30 ± 0.16	3.358	0.001
Average Time to Retreatments (months)	20.53 ± 6.44	17.38 ± 4.50	2.501	0.014
Retreatment for Retinal Hemorrhage	1	7	5.670	0.017
Retreatment for New Angiomas	2	5	1.956	0.162

Table 8. Correlation between baseline angioma characteristics and long-term outcomes

Parameter	Intervention Group (n = 43)	Control Group (n = 37)	X ²	Statistical Significance (p-value)
Baseline Number of Angiomas			12.573	0.002
1-3 Angiomas	30	12		
4-6 Angiomas	10	14		
7+ Angiomas	3	11		
Recurrence Rate by Baseline Angioma Number			4.805	0.028
Fewer Angiomas	2	8		
More Angiomas	41	31		
Recurrence Rate for Posterior Angiomas			0.024	0.877
Posterior	26	23		
Anterior	17	14		

Table 9. Comparison of progression of retinal vascular abnormalities between the two groups

Parameter	Intervention Group (n = 43)	Control Group (n = 37)	t/X ²	Statistical Significance (p-value)
Mean Progression of Retinal Vessels (mm/year)	0.17 ± 0.02	0.28 ± 0.02	28.124	< 0.001
Incidence of Retinal Vascular Abnormalities	5	18	13.306	< 0.001
Changes in Retinal Vessel Diameter (mm)	0.22 ± 0.04	0.30 ± 0.05	8.085	< 0.001
Progression of Retinal Neovascularization	2	11	9.191	0.002
Retinal Vein Occlusion	0	4	4.893	0.027

Table 10. Analysis of factors influencing visual acuity

Variable	B	SE	Wald	P	OR	95% CI
Laser photocoagulation treatment	0.997	0.313	10.140	0.0001	0.369	0.200-0.682
Mean Number of Angiomas	2.079	0.305	46.396	< 0.001	7.999	4.397-14.550
Constant	10.820	4.375	6.115	0.013	0.000	-

acuity. The results indicated that laser photocoagulation (B = 0.997, P = 0.0001) was a significant positive factor, with an odds ratio (OR) of 0.369 (95% CI: 0.200-0.682), suggesting that laser treatment significantly influenced the outcome. On the other hand, the mean number of angiomas (B = 2.079, P < 0.001) was also a significant factor, with an OR of 7.999 (95% CI: 4.397-14.550), indicating a strong correlation with poorer visual outcomes (**Table 10**). This

analysis highlights that both the type of treatment (laser photocoagulation) and the baseline number of retinal angiomas are crucial factors influencing the long-term visual outcomes of patients with VHL syndrome.

Discussion

This study demonstrates the long-term effectiveness of laser treatment for retinal angiomas

in patients with VHL syndrome. Patients in the intervention group showed significantly better visual outcomes, fewer recurrences, less ocular damage, and a higher quality of life compared to those in the control group. These findings suggest that laser photocoagulation is a highly effective approach for treating retinal angiomas in VHL patients, helping to preserve vision and improve overall health. Importantly, this study considers both the ocular and systemic health over time, providing insights that could inform future treatment strategies for VHL patients.

Laser therapy has been shown to improve visual outcomes for patients with retinal angiomas associated with VHL syndrome. The intervention group experienced a significant improvement in visual acuity, a result that aligns with previous studies that have demonstrated that laser photocoagulation improves visual stability in various retinal conditions [11-14]. This improvement is likely due to the laser's ability to coagulate abnormal blood vessels, thereby reducing leakage - a common cause of vision decline [15, 16]. Laser therapy stops retinal bleeding and macular edema, helping to preserve the structural integrity of the retina and maintain vision [17-19]. This means that laser treatment is particularly beneficial for individuals with VHL, who are at high risk for continued retinal damage [20, 21]. These outcomes reinforce the importance of laser therapy for treating retinal angiomas in VHL patients.

As well as improving vision, laser treatment significantly decreases the chances of retinal angiomas recurring, which is crucial for the long-term management of VHL syndrome. Laser therapy seems to provide substantial protection from recurring symptoms in these patients. By utilizing laser photocoagulation, existing angiomas are effectively managed, and formation of new blood vessels in the retina is potentially prevented [22, 23]. The laser's ability to coagulate vessels and block the development of retinal neovascularization is likely responsible for this reduction [24, 25]. In addition, laser-treated individuals experienced a longer period before the next lesion appeared compared to those in the control group, suggesting that the treatment's effects are sustained over time. For patients with VHL syndrome, a slower recurrence of angiomas is

crucial, as rapid retinal growth could lead to vision loss without timely intervention. These findings indicate that laser therapy helps prevent angioma recurrence, reduces the need for additional treatment, and offers a more stable ocular environment for VHL patients.

Compared with the control group, laser treatment demonstrated superior safety, as evidenced by lower incidences of adverse events such as retinal hemorrhage, macular edema, and retinal detachment. The occurrence of vision loss was also significantly lower in the intervention group. These results confirm the safety and efficacy of laser treatment in preventing serious complications associated with retinal angiomas [26, 27]. The lower rates of retinal hemorrhage and macular edema in the intervention group suggest that this therapy not only reduces the size of angiomas and limits neovascularization but also decreases the risk of secondary complications that could lead to irreversible vision loss. This benefit is likely attributed to the precise targeting of laser energy, which effectively acts on abnormal blood vessels while minimizing damage to surrounding healthy retinal tissue [28, 29]. The reduced need for retreatment and the lower incidence of severe ocular complications further highlight the advantages of laser treatment over mere observation [30]. This safety advantage is critical for long-term visual preservation, particularly in diseases like VHL syndrome, which are prone to multiple recurrences and complications that severely impact quality of life.

Using laser therapy can improve both the visual function and overall quality of life in patients with retinal angiomas linked to VHL syndrome. This finding is clinically significant because maintaining eye function without further deterioration can help prevent functional blindness, which would otherwise severely impact a patient's daily life. Moreover, patients in the intervention group showed better performance than those in the control group across multiple quality of life areas, including vision health, physical function, mental well-being, and daily task performance. This improvement is likely to be due to a combination of fewer eye problems and better preservation of vision. Proper or improved vision enhances a patient's ability to perform daily tasks with greater ease, thereby boosting both physical and mental health. The

enhanced protection of the macula and greater retinal sensitivity in the intervention group suggest that laser treatment helps maintain retinal health. By reducing disease progression and strengthening the eyes, laser therapy has a direct, positive effect on a patient's overall well-being. These results demonstrate that laser therapy not only offers effective treatment but also improves the management of VHL syndrome.

Despite these encouraging results, this study has several limitations. First, the data is retrospective, which introduces the possibility of selection bias. Even though the patients were well balanced at baseline, further randomized controlled trials (RCTs) are needed to eliminate selection bias and to confirm that laser treatment leads to superior outcomes. Additionally, the relatively small sample size limits the generalizability of these findings. Larger studies with a more diverse participant pool could provide clear insights into the treatment's efficacy. Finally, the study primarily focused on retinal and ocular outcomes and did not explore potential long-term systemic effects of laser therapy, such as its impact on the kidneys or pancreas.

Overall, laser photocoagulation for retinal angiomas associated with von Hippel-Lindau syndrome can significantly improve visual acuity, reduce recurrence rates, slow the progression of retinal vascular abnormalities, and enhance patients' quality of life. The results of this study suggest that laser therapy is an effective long-term treatment option for retinal angiomas in VHL syndrome. Future prospective studies with larger sample sizes and extended follow-up periods are needed to further validate these findings. Additionally, research should explore the potential impact of laser treatment on the systemic manifestations of VHL syndrome, including renal and pancreatic involvement.

Disclosure of conflict of interest

None.

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