Intraocular VEGF Level as a Risk Factor for Postoperative Complications after Vitrectomy for Proliferative Diabetic Retinopathy

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PURPOSE. To investigate whether vitreous and aqueous humor concentrations of vascular endothelial growth factor (VEGF) predict postoperative complications after vitrectomy for proliferative diabetic retinopathy (PDR).

METHODS. Sixty eyes of 52 patients with PDR who underwent vitrectomy were enrolled. Vitreous and aqueous humor were obtained from eyes with PDR during primary vitrectomy and the levels of VEGF were measured using a commercial flow cytometer. Patients were followed for more than 6 months after surgery. Demographic data and both intraoperative and postoperative findings were recorded. The relationship between VEGF levels in ocular fluids and the main postoperative complications of early vitreous hemorrhage (VH) and neovascular glaucoma (NVG) occurring during follow-up was analyzed. Logistic regression analyses were performed to examine risk factors related to postoperative complications.

RESULTS. Early VH occurred in 25%, and NVG occurred in 8% of 60 eyes. The vitreous levels of VEGF were significantly higher ($P = 0.015$) in eyes with early VH than in those without. The aqueous humor and vitreous levels of VEGF were significantly higher ($P = 0.005$ and $P = 0.001$, respectively) in eyes with NVG than in those without. Axial length was significantly shorter in eyes with early VH than in those without ($P = 0.028$). Multivariate logistic regression analysis showed that the higher vitreous VEGF level was associated with a risk of early VH after vitrectomy for PDR (odds ratio, 5.1; $P = 0.020$).

CONCLUSIONS. High intraocular VEGF level at the time of primary vitrectomy in patients with PDR was identified as a significant risk factor for postoperative early VH. (Invest Ophthalmol Vis Sci. 2012;53:6403–6410) DOI:10.1167/iovs.12-10367

Patients and Methods

Patients

This retrospective study enrolled patients with diabetes who underwent primary pars plana vitrectomy for VH with or without traction retinal detachment secondary to PDR, between April 2007 and March 2008 at Hachiouji Medical Center of Tokyo Medical University, and between June 2008 and May 2010 at Tokyo Medical University Hospital. The study was approved by the institutional review board.

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committee of Tokyo Medical University. Informed consent for surgery and vitreous sampling was obtained according to the Declaration of Helsinki.

The indication for vitrectomy was complications of PDR such as nonclearing VH and/or progressive traction retinal detachment. Exclusion criteria were: (1) a history of prior vitrectomy except laser photocoagulation to treat PDR, (2) a history of intravitreal anti-VEGF antibody injection, (3) preexisting iris and chamber angle neovascularization, (4) posterior capsule rupture during cataract surgery, (5) intraoperative use of silicone oil, and (6) less than 6 months of follow-up after primary vitrectomy.

**Surgical Technique**

All patients underwent standard pars plana vitrectomy under local anesthesia. Vitrectomy was conducted using a 20-gauge 3-port system between April 2007 and March 2008, and a 23-gauge 3-port system between June 2008 and May 2010. Phacoemulsification and aspiration (PEA) were performed simultaneously in patients with cataract, and an acrylic foldable intraocular lens (IOL) was placed in the capsular bag. Vitrectomy was performed with a high-speed vitreous cutter (2500 cycles/min), with intravitreal injection of triamcinolone acetonide to visualize the vitreous gel and vitreoretinal adhesions. Fibrovascular membrane dissection, segmentation, and delamination were performed mainly with vitreoretinal scissors or forceps in 20-gauge vitrectomy, and with a high-speed vitrectomy cutter in 23-gauge vitrectomy, followed by posterior vitreous surface removal. Intraoperative bleeding was controlled either by endodiathermy or increasing the irrigation bottle height. To identify rebleeding from vascular membrane or fragile vessels during vitrectomy, the intraocular pressure (IOP) was decreased until 2 mm Hg at the end of membrane manipulation. If the patient was taking an anticoagulant for underlying systemic diseases, anticoagulant was discontinued 1 week before surgery, and resumed within 1 week after surgery. The vitreous body was removed as far as the vitreous base under scleral depression (vitreous base shaving), and blood clots in the peripheral vitreous skirt were also removed by vitreous base shaving. Endolaser was applied to complete panretinal photocoagulation up to the ora serrata. In some patients with combined traction–rhegmatogenous retinal detachment or retinal detachment caused by iriogenetic tear, fluid-air exchange was performed. In serious cases, 0.5 to 0.8 mL of 100% sulfur hexafluoride (SF₆ gas) was injected at the end of surgery. Patients who had undergone fluid–gas exchange were instructed to remain face down for 3 to 5 days.

**Clinical Data Analysis**

Preoperative, intraoperative, and postoperative data were collected for each patient. Preoperative data at the time of primary surgery included age; sex; duration and status of diabetes mellitus (HbA1C); other systemic diseases such as hypertension and hyperglycemia; renal status (serum creatinine); medications such as anticoagulant for systemic disease; and ophthalmic factors including best-corrected visual acuity (BCVA), lens status, axial length, and IOP. Intraoperative data included the number of PEA and IOL procedures; SF₆ or air tamponade; total number of shots of endolaser photoacoagulation; and the presence or absence of fibrovascular proliferation (FVP), neovascularization of optic disc (NVD), and traction retinal detachment. Postoperative data included BCVA at the final visit; number of episodes of complications such as VH, NVG, and residual retinal detachment; and duration of follow-up in months. Postoperative VH was detected by indirect ophthalmoscopic fundus examination from day 3 after primary surgery until the final follow-up. Vitreous hemorrhage was defined and graded according to previous reports³,⁵,⁷ as follows. Grade 1 was defined as mild VH with visible fundus details; grade 2 as moderate VH with visible optic disc or large vessels; and grade 3 as severe VH with no retinal details and no fundus reflex. In the case of gas-injected eye, the grade of VH was assessed from the fundus status below the gas bubbles. Postoperative recurrent VH was defined as a new episode of VH of grade 1 or above occurring later than 3 days after primary surgery. Both early (<4 weeks) and late (>4 weeks) vitreous hemorrhages were recorded. Vitreous hemorrhage occurring on the first day after surgery was classified as early VH if the hemorrhage developed to grade 2 or above at postoperative day 3. NVG was defined as stromal and chamber angle neovascularization, with IOP elevated to 25 mm Hg or higher. Decimal visual acuity was measured using a Landolt C acuity chart and converted to logarithm of minimal angle of resolution (logMAR) scale. Counting fingers and hand movement were defined as 0.01 (2.0 logMAR) and 0.001 (3.0 logMAR), respectively. Visual improvement was defined as an increase of at least 0.3 logMAR units.

**Sample Collection and Measurements of VEGF**

Aqueous humor (AQH) sample (0.1–0.2 mL) was aspirated from the corneal limbus with a 27-gauge needle attached to a sterile tuberculin syringe at the beginning of surgery. A vitreous sample (0.1–0.5 mL) was removed from the midvitreous with a vitreous cutter at the start of vitrectomy before intraocular infusion. The vitreous and AQH samples were collected into sterile tubes and stored immediately at −80°C, and were assayed within 6 months after collection. Human VEGF in the samples were assayed using a commercial kit (Cytometric Bead Array Flex Kit; Becton, Dickinson and Company, Franklin Lakes, NJ) according to the methods described previously.¹³ Two-color flow cytometric analysis was performed using a flow cytometer (FACSCalibur; Becton, Dickinson and Company). The lowest detectable concentration of this assay was 4.5 pg/mL for VEGF. Any concentrations below this level were recorded as the lowest detectable concentration for statistical analysis.

**Statistical Analysis**

Vitreous and aqueous concentrations of VEGF and clinical data are expressed as median (range). To evaluate the association of postoperative complications with VEGF concentrations and other clinical data described earlier, patients were divided into two groups according to the presence or absence of each postoperative complication. Wilcoxon rank-sum test and χ² test (if n < 5, the Fisher’s exact test) were used to compare VEGF concentrations and other clinical data between two groups. VEGF concentrations with a skewed distribution were transformed to a logarithmic scale and univariate and multivariate logistic regression analyses were performed to identify the independent clinical factors related to the postoperative complication. A value of P < 0.05 was considered statistically significant. All analyses were performed using commercial statistical analysis software (JMP version 5.0.1J; SAS Institute, Cary, NC).

**RESULTS**

**Patient Characteristics**

Patient demographics and preoperative ocular findings are summarized in Table 1.

A total of 60 eyes of 52 diabetic patients (36 males; 16 females) undergoing vitrectomy for PDR complications were studied. Their median age was 58 years (range, 27–84 years). The median duration of diabetes was 14.4 years (range, 6.1–28.2 years), and median hemoglobin (Hb) A₁c level was 7.1% (range, 4.6–12.1%). The median baseline BCVA was 1.69 logMAR units (range, 0.3–3.0), and median IOP was 14.0 mm Hg (range, 9–22 mm Hg). Panretinal photoacoagulation (PRP) had been performed before surgery in 41 eyes (68%). All patients had VH, and 19 eyes (32%) also had traction retinal detachment. The median follow-up period after primary surgery was 17.0 months (range, 6.0–49.0 months).
Surgical Procedures and Outcomes

The surgical procedures and outcome are summarized in Table 2. PEA and IOL implantation were performed in 47 eyes (78%). A 20-gauge vitrectomy was performed in 20 eyes (33%), and 23-gauge vitrectomy in 40 eyes (67%). Fifty-one patients (98%) received additional endolaser photocoagulation, and median total number of shots was 1496 (range, 78–3000). Gas tamponade was conducted in 17 eyes (28%). Final anatomic success rate was 98%. The median postoperative BCVA was 0.3 logMAR units (range, 0.08–2.0), which was improved significantly compared with the median baseline BCVA (P < 0.0001). Postoperative BCVA improved by 3 lines or more in 55 eyes (92%), was unchanged in 4 eyes (7%), and decreased in 1 eye (1%).

The incidence of major postoperative complications was 37%. Recurrent VH occurred in 24 eyes (40%) during follow-up periods. Among them, early VH occurred in 15 eyes (25%), and late VH in 11 eyes (18%). Both early and late VH occurred in 2 eyes (3%). NVG occurred in 5 eyes (8%) and unprogressive focal retinal detachment in 1 eye (2%).

Relation of VEGF Levels and Clinical Data with Early Vitreous Hemorrhage

Vitreous VEGF levels were above the detection limit in 57 of 60 eyes (95%) and below the detection limit in 3 of 60 eyes (5%), whereas AQH samples were above the detection limit in 42 of 60 eyes (70%) and below the detection limit in 18 of 60 eyes (30%). The median VEGF level was 119.2 pg/mL (range, 4.5–1126.6) in the AQH, and 260.8 pg/mL (range, 4.5–7817.9) in the vitreous. A significant positive correlation was observed between the AQH VEGF level and vitreous VEGF level (rs = 0.367, P = 0.004).

Eyes with early postoperative vitreous hemorrhage (VH group) and eyes without early postoperative vitreous hemorrhage (non-VH group) were compared with respect to ocular fluid levels of VEGF and clinical data. The vitreous VEGF level was significantly elevated in the VH group (median, 532.6 pg/mL; range, 4.5–7817.9) than in the non-VH group (median, 256.2 pg/mL; range, 4.5–1588.1) (P = 0.015) (Table 3, Fig.).

Otherwise, the AQH VEGF level was not significantly elevated in the VH group (median, 259.2 pg/mL; range, 4.5–632.6) than in the non-VH group (median, 111.1 pg/mL; range, 4.5–1126.6) (P = 0.123).

The prevalence of hypertension differed significantly between the two groups (87% vs. 56%, P = 0.022), and the rate of hyperlipidemia also differed significantly between two groups (60% vs. 18%, P = 0.002). Axial length in the VH group (median, 22.8 mm; range, 21.0–25.7) was significantly shorter than that in the non-VH group (median, 23.5 mm; range, 21.9–26.9) (P = 0.026) (Table 3). Axial length in PDR patients with preoperative traction retinal detachment (median, 22.7 mm; range, 21.0–25.1) was also significantly shorter than that in patients without traction retinal detachment (median, 23.5 mm; range, 21.1–26.9) (P = 0.022). Likewise, axial length in PDR patients with preoperative FVP (median, 22.8 mm; range, 21.8–26.1) was significantly shorter than that in patients without FVP (median, 24.1 mm; range, 21.1–26.9) (P = 0.018).

Among samples above the detection limit, a weak but significant negative correlation was observed between the AQH VEGF level and axial length (n = 42, rs = –0.39, P = 0.016); otherwise, no significant correlation was observed between the vitreous VEGF level and axial length (n = 57, rs = –0.26, P = 0.07). Other clinical factors, such as oral anticoagulant, traction retinal detachment, FVP, NVD, cataract surgery, and gas tamponade, did not correlate significantly with early VH.

Logistic regression analyses were performed to identify possible risk factors in eyes with early VH (Table 4). The result of univariate logistic regression analysis showed that the vitreous VEGF level (odds ratio [OR], 3.5; P = 0.022), axial length (OR, 1.8; P = 0.030), hypertension (OR, 5.2; P = 0.044), and hyperlipidemia (OR, 6.9; P = 0.003) were significant risk factors for early VH. Next, multivariate analysis was performed...
using vitreous VEGF levels together with the clinical factors indicative of rebleeding tendency such as age, axial length, traction retinal detachment, hypertension, hyperlipidemia, and gas tamponade as independent variables. The result of multivariate logistic regression analysis showed that only an elevated vitreous VEGF concentration increased the risk of early VH (OR: 5.1, P = 0.020).

On the other hand, no significant differences in ocular fluid VEGF levels and clinical data were detected between eyes with late VH and those without this complication.

**Relations of VEGF Levels and Clinical Data with NVG**

Eyes with postoperative NVG (NVG group) and eyes without postoperative NVG (non-NVG group) were compared with respect to the AQH and vitreous levels of VEGF and clinical data. The AQH VEGF level was significantly elevated in the NVG group (median, 106.6 pg/mL; range, 4.5–7817.9) than that in the non-NVG group (median, 10.6 pg/mL; range, 4.5–1126.6) (P = 0.005). The vitreous VEGF level was also significantly elevated in the NVG group (median, 2022.1 pg/mL; range, 801.3–7817.9) than that in the non-NVG group (median, 239.9 pg/mL; range, 4.5–1808.6) (P = 0.001) (Table 5, Fig.). Other clinical factors such as hypertension, traction retinal detachment, NVD, previous PRP, cataract surgery, and additional endolaser photocoagulation did not correlate significantly with NVG. Risk analysis was not conducted for postoperative NVG due to the small number of patients (5 of 60 patients) developing this complication.

**DISCUSSION**

Early VH may occur even after anatomically successful vitrectomy for PDR, with rates ranging between 17% and 63%, and the incidence is still high despite recent technical advances in vitrectomy. Many clinical reports described new bleeding from fibrovascular membrane with tangential or vertical traction from the residual vitreous, and proposed that fibrovascular membranes transected at surgery and fragile vessels may cause early VH after vitrectomy for PDR. However, no previous reports have evaluated the significant risk factors for early VH after vitrectomy for PDR, except the severity of diabetic retinopathy and age. VEGF is the pivotal angiogenic growth factor that activates endothelial cells to migrate, proliferate, and form capillaries. Many studies have reported the importance of VEGF in the pathologic angiogenesis of PDR. The vitreous VEGF concentration is increased in patients with PDR, and is higher in active diabetic retinopathy than in inactive diabetic retinopathy. Another study showed that an increased extent of membrane peeling, which reflects the difficulty of vitrectomy and high activity of PDR, increases the possibility of early postoperative VH in PDR surgery. These findings would suggest that patients with high ocular fluid VEGF levels before vitrectomy have high neovascular activity and extensive proliferative changes, and therefore may be more susceptible to develop early postoperative VH. However, in our logistic regression analyses, only the preoperative vitreous VEGF level was identified as a significant risk factor (OR: 5.1), whereas NVD, traction retinal detachment, and FVP were not significant risk factors. In this study, we excluded cases with preexisting iris and chamber angle neovascularization and cases with severe proliferation requiring intraoperative silicone oil injection. These excluded cases likely contained many with severe PDR, and their exclusion may have affected the frequency of postoperative complications. Therefore, the possibility of selection bias with respect to severity has to be considered in interpreting the results of this study. Nevertheless, our study demonstrated a novel finding that a high preoperative intraocular VEGF level might be prominently involved in early postvitrectomy VH. To validate the results of the present study, we have planned a prospective study with a larger number of patients.

The exact mechanism of how a high preoperative VEGF level is associated with early postoperative VH is unclear from the results of our study. Several studies have demonstrated that adjunctive use of an intravitreal bevacizumab (IVB) injection is beneficial to reduce the rate of early VH after vitrectomy for PDR. Preoperative use of IVB in vitrectomy for PDR may further facilitate hemostasis during fibrovascular membrane manipulation, and shorten operating time. Facilitated hemostasis is likely related to the antiangiogenic effect of bevacizumab. Reduction of the postoperative early VH rate by IVB might be associated with improved hemostasis during vitrectomy. In patients who show high VEGF expression before vitrectomy, it is possible that the potential VEGF expression ability is also high early after PDR surgery. Ahn et al. reported that IVB injection at the end of vitrectomy significantly
reduced the incidence of early postoperative VH in PDR. Considering their results and the present findings, overexpressed VEGF in the eye after vitrectomy may be an important factor causing early VH. We speculate that during the early postvitrectomy stage, direct actions of intraocular VEGF or indirect actions mediated by other cytokines, such as suppressed repair mechanisms of residual new vessels or retinal vessels damaged during surgery and the fibrinolytic activity of VEGF,16 may induce early postoperative hemorrhage. Interestingly, perioperative IVB has been shown to be ineffective in reducing the incidence of late VH.27 This result supports our finding of no significant relation between preoperative intraocular VEGF concentration and late VH. The effect of intraocular VEGF on early postoperative VH is unclear. Moreover, to what extent the pharmacologic actions of bevacizumab are maintained in the vitrectomized eye after pre- or intraoperative IVB injection remains unknown. Nevertheless, the present study supports perioperative IVB injection for the prevention of early VH after vitrectomy for PDR. Furthermore, Funatsu et al.17 demonstrated that the preoperative ocular fluid levels of VEGF correlate with the progression of PDR and the outcome of vitreous surgery, and proposed that measurement of VEGF before surgery may be useful for predicting the outcome of PDR surgery. Similarly, our results also suggest that measurement of the preoperative vitreous VEGF level may be useful for predicting early VH and NVG after vitreous surgery for PDR.
Intraocular tamponade with long-acting gases such as perfluoropropane (C₃F₈) has been reported to be a useful adjunct to vitrectomy for PDR in the reduction of early VH. In the present study, intraocular gas tamponade with SF₆ did not reduce the incidence of early VH. Consistent with our result, Koutsandrea et al. also reported that SF₆ tamponade did not prevent postoperative VH. Compared with C₃F₈, SF₆ that we used in this study is more rapidly absorbed in the eye and therefore does not provide an adequate mechanical tamponade effect on the fragile vessels, which may have accounted for the failure to prevent early VH. The fact that use of SF₆ gas is not a factor that affects the rate of postoperative VH is an important finding from the viewpoint of reliability of the present analysis.

An important finding of the present study is that shorter axial length is associated significantly with a higher incidence of early postoperative VH. Diabetic patients with retinopathy have shorter axial length than those without retinopathy. Furthermore, eyes with myopic spherical equivalent refraction and longer axial length are associated with a lower risk of moderate diabetic retinopathy and vision-threatening diabetic retinopathy. This is the first report of a relation between the rate of early VH after vitrectomy and axial length. When we analyzed the relationship between axial length and the fundus conditions of PDR, axial length was significantly shorter in PDR patients with concurrent hypertension, VEGF and other intraocular fluid VEGF concentration cannot be elucidated in the present study, further investigations are required in the future.

In this study, the incidence of early VH was high in patients with hypertension and hyperlipidemia. Epidemiologic studies have clearly shown that systemic hypertension is an independent risk factor for diabetic retinopathy. Observational and epidemiologic studies support an association between diabetic retinopathy with elevated serum lipids. Results suggest a possible relation between these two systemic diseases and PDR. The effect of hypertension and hyperlipidemia on the development of early postoperative VH has not been reported, and the associations could not be explained from the present study. However, a previous study has reported that vitreous concentrations of MCP-1 and IL-8 are elevated in diabetic retinopathy concurrent with hypertension. Suzuma et al. demonstrated that exposure of bovine retinal endothelial cells to cyclic stretch upregulated the expressions of VEGF and its receptor, whereas retinal expressions of VEGF and its receptors were also increased in spontaneously hypertensive rats. These findings suggest that in PDR with concurrent hypertension, VEGF and other intraocular factors that exacerbate retinopathy may be overexpressed.

### Table 4. Logistic Regression Analyses of Risk Factors Associated with Early Vitreous Hemorrhage

<table>
<thead>
<tr>
<th>Analysis (n = 60)</th>
<th>Factors</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate logistic regression</td>
<td>AQH VEGF levels (log 10 pg/mL)</td>
<td>1.3 (0.60–2.87)</td>
<td>0.485</td>
</tr>
<tr>
<td></td>
<td>Vitreous VEGF levels (log 10 pg/mL)</td>
<td>3.5 (1.06–11.9)</td>
<td>0.022</td>
</tr>
<tr>
<td></td>
<td>Axial length</td>
<td>1.8 (1.06–3.22)</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
<td>5.2 (1.05–25.78)</td>
<td>0.044</td>
</tr>
<tr>
<td></td>
<td>Hyperlipidemia</td>
<td>6.9 (1.92–25.08)</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Gas tamponade</td>
<td>2.1 (0.60–7.10)</td>
<td>0.252</td>
</tr>
<tr>
<td>Multivariate logistic regression</td>
<td>Vitreous VEGF levels (log 10 pg/mL)</td>
<td>5.1 (1.29–20.35)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

### Table 5. Neovascular Glaucoma after Surgery and Clinical Data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PDR with NVG (n = 5)</th>
<th>PDR without NVG (n = 55)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AQH VEGF levels (pg/mL)</td>
<td>500.9 (120.0–652.6)</td>
<td>106.3 (4.5–1126.6)</td>
<td>0.005</td>
</tr>
<tr>
<td>Vitreous VEGF levels (pg/mL)</td>
<td>2022.1 (801.3–7817.9)</td>
<td>239.9 (4.5–1808.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (y)</td>
<td>62 (45–69)</td>
<td>58 (27–84)</td>
<td>0.239</td>
</tr>
<tr>
<td>HbA₁C (%)</td>
<td>7.7 (6.5–9.1)</td>
<td>7.1 (4.6–12.1)</td>
<td>0.218</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7 (60%)</td>
<td>35 (63%)</td>
<td>0.866</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1 (20%)</td>
<td>16 (29%)</td>
<td>0.666</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.62 (0.44–0.99)</td>
<td>0.85 (0.21–8.70)</td>
<td>0.086</td>
</tr>
<tr>
<td>Oral anticoagulant</td>
<td>2 (40%)</td>
<td>11 (20%)</td>
<td>0.351</td>
</tr>
<tr>
<td>Traction retinal detachment</td>
<td>0 (0%)</td>
<td>19 (35%)</td>
<td>0.112</td>
</tr>
<tr>
<td>Previous PRP</td>
<td>4 (80%)</td>
<td>37 (67%)</td>
<td>0.558</td>
</tr>
<tr>
<td>Fibrovascular proliferation</td>
<td>2 (40%)</td>
<td>29 (53%)</td>
<td>0.585</td>
</tr>
<tr>
<td>Neovascularization of the disc</td>
<td>3 (60%)</td>
<td>30 (55%)</td>
<td>0.814</td>
</tr>
<tr>
<td>Cataract surgery (PEA + IOL)</td>
<td>5 (100%)</td>
<td>42 (76%)</td>
<td>0.194</td>
</tr>
<tr>
<td>20-gauge system</td>
<td>2 (40%)</td>
<td>18 (33%)</td>
<td>0.611</td>
</tr>
<tr>
<td>Additional endolaser photocoagulation (total shot)</td>
<td>1342 (150–2320.0)</td>
<td>1500 (78–3000)</td>
<td>0.261</td>
</tr>
<tr>
<td>Gas tamponade</td>
<td>0 (0%)</td>
<td>17 (31%)</td>
<td>0.142</td>
</tr>
<tr>
<td>Triamcinolone acetone</td>
<td>4 (80%)</td>
<td>32 (58%)</td>
<td>0.341</td>
</tr>
</tbody>
</table>

Data are expressed as number (% of eyes, or median (range).
as a result of hypertension, which may result in an increased risk to develop early postoperative VH.

The second important result of this study is that the intraoperative intravital VEGF concentrations were significantly higher in patients who developed postoperative NVG. Apart from intravitreal VEGF levels, no other clinical factors examined in the present study were significantly related to the occurrence of postoperative NVG. Despite the recent advances in vitrectomy surgery, 2 to 12% of patients develop NVG after PDR surgery. In the present study, 5 eyes (8%) had postoperative NVG. Preexisting rubecosis,59 intracapsular cataract surgery,50 and postoperative retinal detachment58 have been reported to be risk factors for NVG after PDR surgery. Kadonosono et al.59 reported that vitrectomy combined with phacoemulsification and intracapsular lens implantation significantly reduced the incidence of postoperative iris and angle neovascularization, and this favorable result might be related to improved visualization during surgery, more complete excision of peripheral vitreous, and more complete endolaser photocoagulation. All the subjects in the present study had no iris and angle neovascularization before surgery, and patients who had postoperative NVG had no residual retinal detachment and all underwent simultaneous PEA and IOL implantation. In addition, endolaser photocoagulation was conducted as far as the peripheral retina in all NVG cases, with a mean of 1342 shaving. Therefore, the results of our investigations suggest that a high intraocular VEGF level may be the most important factor associated with the occurrence of postoperative NVG. The vitreous body was removed as far as the vitreous base under scleral depression (vitreous base shaving). Even after washing out the aggravating factors in the vitreous body and applying adequate photocoagulation, the potential ability of VEGF expression may not be reduced immediately. Especially in eyes that express VEGF abundantly before surgery, overexpression of VEGF likely continues after surgery. Thus vitreous surgeons have to be aware of the fact that with the standard vitrectomy used currently, a few percent of patients will develop NVG after surgery. However, since we had only five cases of postoperative NVG, the analysis is by no means conclusive. Further study on a large number of patients and investigation of whether perioperative IVB prevents the occurrence of postoperative NVG are required in the future.

In conclusion, high vitreous and aqueous humor levels of VEGF at the time of primary vitrectomy in patients with PDR were identified as significant risk factors for early postoperative VH and NVG. These results support the perioperative use of intravitreal anti-VEGF antibody injection in patients undergoing vitrectomy for PDR, for the prevention of postoperative complications. Furthermore, measurement of VEGF levels in ocular fluids may be useful for predicting the occurrence of postvitrectomy complications in patients with PDR.

References


