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PROMPT VITRECTOMY IN PATIENTS WITH TYPE 1 DIABETES AND DIABETIC RETINOPATHY

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Abstract

Objectives: To evaluate the long-term outcomes of patients with type 1 diabetes mellitus (DM) who underwent prompt vitrectomy and to discuss the optimal timing for surgery.

Methods: This retrospective study included diabetic retinopathy (DR) patients with type 1 DM who underwent prompt vitrectomy at Retina Ophthalmic Research Center between March 2015 and January 2020. Demographical and clinical features including duration of diabetes, visual loss and follow-up time between visual loss and vitrectomy, best corrected visual acuity (BCVA), reoperations, complications, were reviewed.

Results: There were 25 eyes of 18 patients (with a mean age of 33 years). Duration of diabetes was 14.2 years. Mean follow-up was 23.1 months. 19 eyes received intravitreal dexamethasone implant and 5 eyes received intravitreal triamcinolone injection in the first surgery. Mean preoperative BCVA was improved from 0.3 to 0.7 log-mar postoperatively (p=0.002). Anatomic success was achieved in 23 eyes. Visual acuity was improved in vision safely and efficiently.19 eyes, stabilized in 4 eyes and deteriorated in 2 eyes. Cataract removal was needed in 6 eyes and retinal detachment occurred in 1 eye.

Conclusions: Prompt vitrectomy in type 1 DM patients is safe and effective which provides long term visual stabilization, high quality of life with low complication rate.

Keywords: Diabetic retinopathy, hemorrhage, prompt, vitrectomy, vitreous



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Introduction

Diabetic retinopathy (DR) is one of the most important causes of blindness in young working population.1 All of type 2 and 60% of type 1 diabetes mellitus (DM) patients will have diabetic retinopathy following 20 years of diagnosis.2 Significant percent of them will have vision threatening retinopathy, approximately one third of patients will have vitreous hemorrhage (VH) which requires vitrectomy surgery maximum conventional despite the treatment.3,4 Particularly, type 1 DM patients are young and need regular lifelong ophthalmological examinations.5 The focus of the treatment in these patients should be long term stabilization with the help of cost effective medical and/or surgical interventions. However, when and which intervention improves the visual acuity in long-term, provides high quality life as well as decreases the economic burden is still controversial. Furthermore, there are only a few studies regarding optimal timing in type 1 diabetic patients with VH.6-14 Diabetic Retinopathy Vitrectomy Study (DRVS) showed that early vitrectomy yielded high anatomical and functional success without increasing the complication rate particularly in type 1 diabetes group who had VH and less than 20 years of diabetes.12-14 Yet, this study was conducted thirty years ago, and endolaser treatment was not part of the surgery done in the study which helps to improve the outcomes and decreases recurrence rates.15 Besides, currently, cutter rate is nearly tenfold faster, illumination is more effective and allows to evaluate the retina, particularly the periphery, widely and surgery is now minimally invasive including 25-27 gauge approaches.9,10,16 There are preoperative intravitreal injection options including corticosteroid agents such as triamcinolone acetonide which improve the DR severity in short-term or dexamethasone implants in long-term.17-21 These modern developments in surgical techniques have improved outcomes and decreased the rate of intraoperative and postoperative complications while also decreasing the duration of surgeries in real life.9,22 Postoperative outcomes were better with prompt vitrectomy and apart from effective clinical outcomes, previous studies regarding early and prompt vitrectomy in DR patients with type 1 DM demonstrated that it was highly cost-effective comparing to the conventional treatments and deferral vitrectomy.7,23,24 Furthermore, Fassbender et al.9 suggested that there is no need to postpone a procedure which will improve the patients'

In this article, we aimed to discuss the optimal time of vitrectomy and evaluate the long-term outcomes of prompt vitrectomy on patients with type 1 DM. Retinal

Materials and Methods

We retrospectively reviewed the medical records of 18 consecutive DR patients with type 1 DM who underwent prompt vitrectomy at Retina Ophthalmic Research Center between March 2015 and January 2020. The study was approved by the institutional review board (0006-2020) and conducted in adherence to the tenets of the Declaration of Helsinki. Demographical and clinical features including age, sex, duration of diabetes, duration of vision loss, time between visual loss and vitrectomy, preoperative best corrected visual acuity (BCVA), presence of previous photocoagulation, intraoperative (bleeding, retinal breaks) and postoperative complications (reoperation, rise in intraocular pressure, cataract) were reviewed from medical charts.

Phakic type 1 DM patients younger than 50 years of age with at least 6 months follow-up were included in this study. Visual acuity did not have an impact on decision of surgery. Prompt vitrectomy described as if surgery was performed within 2 months from baseline visit. Prompt vitrectomy indications included attached retina with limited traction, VH, no prior or limited panretinal photocoagulation treatment, progressive retinal ischemia at 2 last visits, early proliferative DR. All patients underwent detailed ophthalmological examination including best corrected visual acuity, anterior segment biomicroscopic evaluation, intraocular pressure measurements, dilated fundus examination, optical coherence tomography (OCT) (Optovue, Inc., Freemont, CA), fundus fluorescein angiography (FFA) (Optovue, Inc., Freemont, CA) and fundus photography (Topcon, Japan).

Three port, 23 or 25 gauge vitrectomy was performed using Dutch Ophthalmic Research Centre Vitrectomy Machine (DORC, Zuidland, the Netherlands) in all patients. Anterior vitreous clearance, core vitrectomy, detailed peripheral vitrectomy, posterior hyaloid removal and fibrovascular membrane dissection were performed with the help of vitrectomy probe, forceps and scissors. Triamcinolone acetonide was used as needed during this procedure for staining the vitreous. Membrane blue was injected for identifying the internal limiting membrane (ILM), and manuel ILM peeling with Eckardt End Gripping Forceps forceps (DORC International, Zuidland, Netherlands) was performed in all patients around macular area limited in vascular archs. Panretinal photocoagulation was applied with 3600 scleral depression. Fluid-air exchange and 20% SF6 gas was used in all cases followed by hemorrhagic control with diathermy in required cases. Patients received either intravitreal injection of triamcinolone or dexamethasone implant. Dexamethasone phosphate and gentamicin were injected subconjunctivally at the end of surgery. Each patient received topical antibiotic drops for one week and steroid drops for a month. Topical steroid drops tapered weekly through 4-week period. Patients were evaluated at day 1, day 7, day 30 following the surgery. Following visits were decided based on the clinical findings of the patients.

Best corrected visual acuity, anterior and posterior segment biomicroscopic evaluation, intraocular pressure measurements, dilated fundus examination, optical coherence tomography and fundus photography were assessed at each visit. Visual acuity was then converted from decimal to logMAR for statistical analysis purposes. Postoperative complications, duration of follow-up visits, the need for reoperations, photocoagulation and intravitreal injections were also noted

Statistical analysis was performed using SPSS® v23.00 for Windows. Data were analyzed using Mann Whitney U and t tests when appropriate and p<0.05 was considered statistically significant.

Results

There were 25 eyes of 18 patients (12male, 6 female) with a mean age of 33 years. Duration of diabetes was 14.2 years. Previous photocoagulation was present in 14 (50%) eyes. Mean follow-up was 23.1 months. 19 eyes received intravitreal dexamethasone implant, whereas 5 eyes intravitreal triamcinolone injection in the first surgery. Preoperative BCVA improved from 0.3 to 0.7 (0.52 to 0.15 logMar: 59 to 77 letters in postoperatively (p=0.002). Anatomic success was ETDRS) achieved in 23 (92%) eves. Anatomic failure was due to neovascularization with glaucoma and hypotony in 2 (8%) eyes as observed in the long-term follow up visits. Visual acuity was improved in 19 eyes, stabilized in 4 eyes and deteriorated in 2 eyes. Deterioration was due to glaucoma and hypotony. Reoperation was required in 3 eyes. Cataract removal was needed in 6 eyes (3 of them combined) following with a mean duration of 7 months. Retinal detachment occurred in 1 eye. Panretinal photocoagulation was added to 4 eyes. Intravitreal antiVEGF injection was performed in 5 eyes with a mean number of 4 times.

Case 1 is a 26-year-old man admitted to our clinic with blurred vision in both eyes for 25 days. He had type 1 DM since 11 years of age. He had been examined by different ophthalmologists several times and diagnosed as nonproliferative diabetic retinopathy. He had no previous treatment in terms of intravitreal injections or laser because, in his story, the visual acuities were perfect. At baseline visit, his BCVA was 0.5 (0.30 logmar:70 letters in ETDRS) in OD and 0.8 (0.10 logmar: 80 letters in ETDRS) in OS. Slit lamp examination was unremarkable. Intraocular pressure was 12 mmHg in OD and 14 mmHg in OS. Dilated fundus examination revealed early proliferative DR in both eyes with mild VH. Optical coherence tomography images indicated that both macula were attached and limited changes in thickness occurred (Figure 1a and 1b). Fundus flourescein angiography showed retinal hemorrhage, venous beading in, absence of a wide range of capillary perfusion area in all quadrants. (Figure 2a,2b,2c and 2d). Patient's right eye underwent vitrectomy with intravitreal implantation of Ozurdex at 2nd week following examination. 25G pars plana vitrectomy was started with four trocares under chandelier. Total vitrectomy was performed, posterior hyaloid was removed and panretinal endophotocoagulation with scleral depression and gas injection was implemented. Internal limiting membrane around the macular area ws peeled.

Patient was recommended to stay at prone position during the early postoperative period. Four weeks following the surgery, his BCVA was 0.9 (0.05 logmar : 83 letters in ETDRS) and his dilated fundus exam revealed the macula and retina totally silent except very few scattered microaneurisms on the temporal side of the macula. In OCT, macular thickness was better and minimal fluid was seen in the macular area (Figure 3). During the 13 months long postoperative follow-up, his visual acuity remained stable and he did not need any intravitreal injections or additional laser treatments

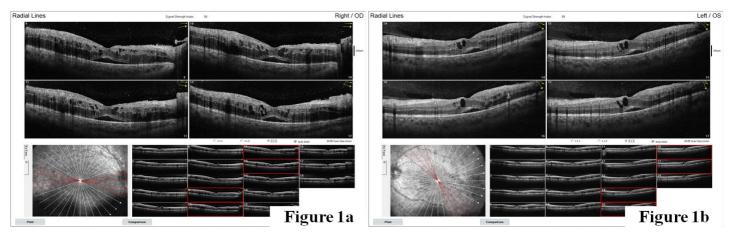


Figure 1a. Optical coherence tomography image of right eye.

Figure 1b. Optical coherence tomography image of left eye

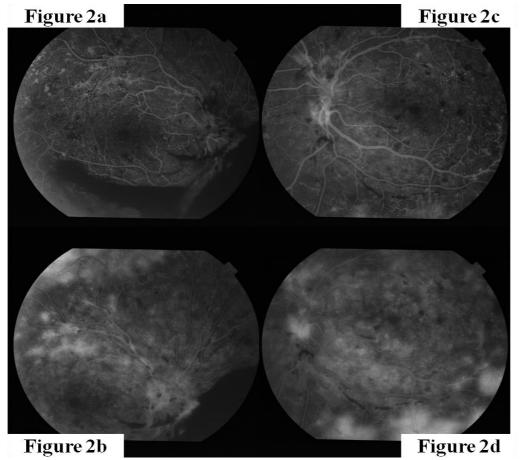


Figure 2. Fundus florescein angiography of bothy eyes showed retinal hemorrhage, venous beading and neovascularization. Fundus florescein angiography of the right eye (2a and 2b) and of the left eye (2c and 2d)

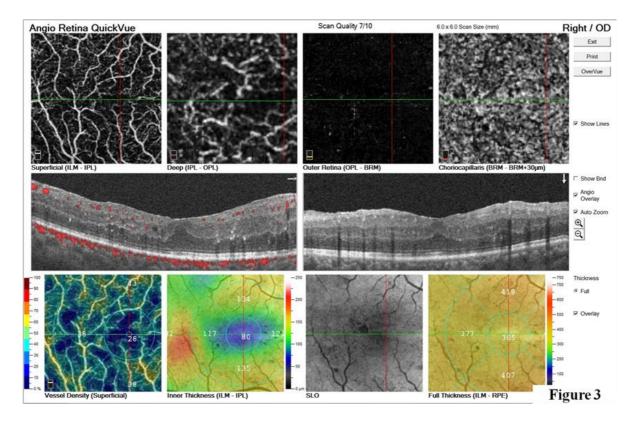


Figure 3. Optical coherence tomography image of right eye, postoperatively.

His left eye also was operated almost 2 months later than right with the same procedures because of the mild VH with early proliferations and preoperative tvisual acuity 0.65 (0.20 logmar : 75 letters in ETDRS) improved to 0.85 (0.07 logmar : 81 letters in ETDRS) after 11 months of surgery. He had some microaneurisms around the temporal macular area without leakage to centrum. OCT was very silent with normal thickness.

Case 2 is a 42 years old male admitted to our hospital with a blurred vision in his left eye for four days. He was diagnosed as type 1 DM 26 years ago. His HbA1c level was 7.6. His BCVA was 0.2 (0.70 log mar : 50 letters in EDTRS) in OD and 0.6 (0.22 logmar: 74 letters in ETDRS) in OS. His slit lamp examination and intraocular pressure were normal in both eyes. His dilated fundus exam revealed very limited hemorrhage in the right eye and VH in OS (Figure 4a and 4b). Neovascularisation of the disc and elsewhere were observed. Optic coherence tomography images could not be obtained from OS. His left eye underwent vitrectomy and intravitreal Ozurdex implant was injected at the end of the surgery. The surgery in the right eye started with 25 G four trocars with chandeliers and total vitrectomy, posterior hyaloid removal, ILM peeling with Trypan Blue and endophotocoagulation with scleral depression, fluid - gas exchanged were performed and dexamethasone implant was injected in the vitreous cavity. After two weeks, the same procedure was performed on his right eye. Three years postoperatively, BCVA was stable with 0.9 (0.05 logmar : 83 letters in ETDRS) in the right eye, 0.7 (0.15 logmar : 77 letters in ETDRS) in the left eye.

Funduscopic exam and OCT data were very silent with regular thickness and no more intravitreal injections or laser treatments were needed at this point (Figure 5). In the right eye, he had a very

subtle lens opacity which was followed regularly. Figure 4. Color fundus photography of both eyes. Color fundus photography of the right eye revealed limited vitreous hemorrhage (4a). Color fundus photography of the left eye revealed vitreous hemorrhage (4b).

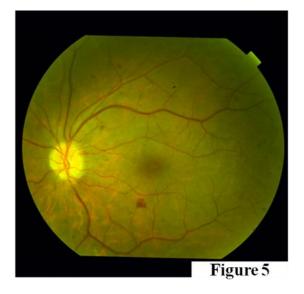


Figure 5. Colour fundus photography of left eye, at postoper ative 6th month.

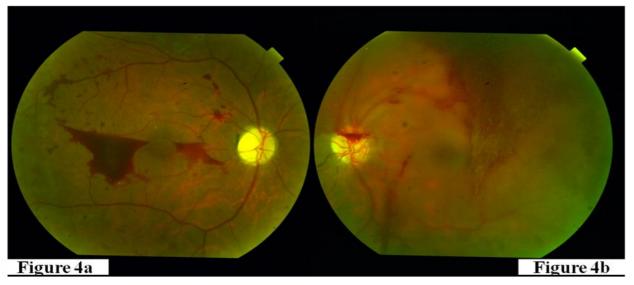


Figure 4. Color fundus photography of both eyes. Color fundus photography of the right eye revealed limited vitreous hemorrhage (4a). Color fundus photography of the left eye revealed vitreous hemorrhage (4b).

Discussion

Nearly one third of type 1 DM patients will develop vision threatening diabetic retinopathy during their lifetimes and will require aggressive conventional or surgical treatment to stabilize their vision.25 Since these patients have long life expectancy, therapeutic approaches should focus to increase their quality of life and provide a long-term solution in a costeffective manner. Diabetic vitrectomy is generally scheduled approximately 3 months later in diabetic patients with VH to give a chance for spontaneous clearance.26 As VH is absorbed, these patients usually receive panretinal photocoagulation with intravitreal injections.27 However, in a recent randomised clinical trial, patients who underwent intravitreal injections followed by panretinal photocoagulation showed more than two fold recurrence rate even though the mean final BCVA was similar compared to the early vitrectomy group.11 This brings up a question: what should be the algorithm and timing from conventional treatment to surgical intervention and what is the best option for each patient?

The advantages of early vitrectomy was proposed since the beginning of 1980s.6-15 Shea et al.6 suggested performance of early vitrectomy before substantial visual loss or tractional retinal detachment development in proliferative DR patients with elevated neovascularization according to their study. Early vitrectomy yielded prompt recovery without increasing the complication rate and poor visual outcome regarding DRVS result.12-14 The number of patients with visual acuity better than 20/40 was significantly higher in the early vitrectomy group (25%) than the delayed vitrectomy group (15%). In addition, early vitrectomy gave higher chances to achieve 10/20 or better visual acuity in these eyes during 4 years follow up although endolaser was not part of the treatment protocol.14 Ramsay et al.7 founded statistically higher anatomic success rates, three times fold reading visual function. They argued that this success might be due to the following reasons: retina was thicker and elastic which allowed safe manipulations during surgery and decreased the rate of iatrogenic retinal breaks, fibrovascular membranes were less complex permitting easier dissections and macula was more functional since permanent alterations were less likely to develop in the initial phases. They also observed decreased risk of anterior segment neovascularization in the early vitrectomy group.7 Studies showed vitrectomy increased the oxygen levels significantly around the lens and the vitreous, decreased VEGF concentration and cytokines significantly around premacular area and had beneficial effects on retinal ischemia.28,29 That may explain why patients who underwent early vitrectomy developed less neovascularization.

Additionally, Ohanley et al.⁸ reported patients who did not undergo vitrectomy within 1 month developed late macular traction and could not reach 6/12 or better. They emphasized not just early but prompt vitrectomy was the reasonable approach to prevent formation of fibrous traction and eliminating the stimulus with the help of removing the scaffold.

Since these studies, the concept of pars plana vitrectomy has changed with advanced technological developments.3031 Current sclerotomies are minimally invasive which allows transconjunctival sutureless up to 27 gauge vitrectomy. Surgical instruments are now more precise and have different types of tips such as straight, curvy, blunt, tapered or sharp that allow to dissect membranes more effectively and precise. Cutter rate can reach up to 16000 cuts/min from 20-27 gauge with various diameters, remove the vitreous rapidly and decrease the duration of surgery.^{16,30,31} Besides, endolaser is now an essential step of vitrectomy. It reduces the recurrence rate of VH from 48% to 7%.15 Panretinal photocoagulation may be applied to the most peripheral parts of retina with the help of wide illumination systems such as chandelier or curved illuminator probe itself with scleral depression. Different types of tips are available including straight or curves, which provide easier access to the peripheral retina.^{30,31} Endolaser burns are not interrupted by media opacities and they can be created at any condition in attached retina. They are more effective than transpupiller laser burns.32-34 According to our experiences also, endolaser application with illuminated probes are very well controlled and the coagulation effects are more effective than transpupillary burns especially in the same power levels. These might be the causes of lower recurrence rates in VH patients who underwent vitrectomy in previous studies.9,11 Moreover, coagulation by endodiathermy may be applied to neovascularised areas to minimize the hemorrhage risk. Just before the conclusion of the surgery, we control if there is any hemorrhagic focus with transient hypotony and use endodiathermy to stop the potential hemorrhages, if there are any. In a recent study, immediate vitrectomy with endolaser decreased the spent time with vision loss and the need for additional panretinal photocoagulation treatment.9 Immediate vitrectomy improved the quality of life of the patients and shortened the period to return back to work in young population.9

Studies showed ILM peeling helps the macular edema to resolve since it may reduce the tangential traction and it contains inflammatory cells in inner surface.35-38 However, a metaanalysis showed vitrectomy with or without ILM peeling did not have any significant effect on postoperative BCVA.39 Besides, removing ILM is particularly controversial in nontractional diabetic macular edema patients and did not improve visual acuity significantly.³⁹⁻⁴¹ The facts remain that, the need for intravitreal injections for DME following vitrectomy with or without ILM peeling should be studied. A Cochrane database reported the prevalence of diabetic macula edema up to 65%.42 Besides, panretinal photocoagulation may also cause changes in patients without clinically significant macular edema.43 We think it is reasonable and removed ILM and posterior hyaloid membrane in all eyes to have a quiet macula. Panretinal photocoagulation induces inflammation and macular thickening and patients received about 2000 laser spots intraoperatively. In our study, due to VH, we could not obtain OCT images in most of the patients. Intraoperative OCT has also introduced which gives a chance to make OCT guided ILM peeling decision during surgery.⁴⁴ Currently, OCT guided ILM peeling is not used widely in clinical practice, so we were not able to use it in our study. In the future, we believe it is going to constitute a very important step of the surgery. On the other hand, we preferred to make intravitreal steroids instead of anti-VEGF injections to control the inflammation which was induced due to endolaser and surgical trauma as well. Intravitreal corticosteroids delay the progression of DR since they reduce cytokine production and VEGF expression which is the key agent for neovascularization development.17,20 Dexamethasone implants are slow releasing drugs and may maintain drug concentrations up to 6 months.17 They decrease the peripheral ischemia in patients with diabetic macular edema and recent studies showed they also improved the severity of the disease.20,45 Besides, dexamethasone seems to have a lower side effect profile, since it is less lipophilic and has a lesser tendency to accumulate in the trabecular meshwork and the lens.⁴⁶ However, these implants are expensive. Patients who could not afford dexamethasone implants received intravitreal triamcinolone injections. During the follow-up, 20% of the patients needed intravitreal injections of dexamethasone implant with a mean number of one time a

year approximately. We think these corticosteroid injections decreased monthly anti-VEGF injection requirements.^{47,49}

Rate of cataract development following diabetic vitrectomy is lower than patients who underwent surgery with other indications.⁵⁰ We observed 6 eyes who had clinically significant cataract and needed surgery. One possible cause may be the age of patients was relatively younger than the patients with other indications. These patients underwent early vitrectomy and surgery was relatively faster than in patients who had more complex fibrovascular and though membranes.⁷ We believe shorter duration of surgery should have an impact on low cataract rates.

On the other hand, diabetes is a chronic disease and type 1 DM patients are a young, working population whose treatment have significant economic impacts.^{23,24} Compared to deferral vitrectomy, early vitrectomy is considered to be extremely cost-effective.²⁴ The number of visits during waiting clearance of VH was found to be 7.43 times greater than the cost to the immediate vitrectomy group.⁹ Prompt vitrectomy obviously decreases the number of additional visits and treatments.

The main advantages of the prompt vitrectomy surgery in type-1 diabetic cases with vitreous hemorrhage are to keep higher levels of visual acuity with a reasonable quality of life by a technique involving total vitrectomy with extensive panretinal endolaser combined with peeling of the ILM and conclusion of the surgery with long lasting steroid implant. In the long-term, obtaining higher quality of life and lowering the burden of disease are the main targets of the treatment modalities in those special cases.

Study Limitations

One of our limitations is the retrospective nature of this study and we did not have a control group.

Conclusion

In conclusion, prompt vitrectomy in type 1 DM patients is safe and effective which provides long-term visual stabilization with low complication rates. Long-term stabilization will yield a high quality of life in this population. Future randomized controlled studies with larger sample sizes are needed to reach more reliable outcomes.

Conflict of interests

The authors declare that there is no conflict of interests.

Data availability statement

The data that support the findings of this study areavailable from the corresponding author upon reasonable request.

Funding

None.

Study association

This study is not associated with any thesis or dissertation work.

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