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# **Continuing Medical Education:**

Long-term visual and retinopathy outcomes in a predominately type 2 diabetic patient population undergoing early vitrectomy and endolaser for severe vitreous haemorrhage G Ratnarajan, F Mellington, M Saldanha, SR de Silva and L Benjamin

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#### Learning objectives

Upon completion of this activity, participants will be able to:

- 1. Identify factors associated with the pathogenesis of proliferative DR
- 2. Describe the type of diabetes for which visual benefits of vitrectomy and endolaser for DR have been demonstrated
- 3. Identify the type of improvement seen with vitrectomy and endolaser treatment for types 1 and 2 DR
- 4. Describe the proportion of diabetic patients with non-macular tractional retinal detachment at the time of vitrectomy

#### Authors/Editors disclosure information

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### Abstract

*Purpose* To evaluate the long-term visual outcome of type 2 diabetic patients receiving early vitrectomy and endolaser for severe vitreous haemorrhage (VH).

Materials and methods Retrospective case note review of 88 eyes (69 type 2 diabetics and 19 type 1 diabetics) of 80 patients who underwent vitrectomy and endolaser within 6 months of VH. Post-operative and most recent VA, in addition to long-term retinopathy grading, were analysed. A subset of patients fulfilling the criteria for the Diabetic Retinopathy Vitrectomy Study was compared with this study. Results Mean pre-operative visual acuity (VA) in the type 2 group was 0.64 logMAR, with 1 eye showing perception light (PL), 10 eyes detecting hand movements (HMs), and 7 eyes counting fingers (CFs). At the 2-week post-operative visit, the mean VA had improved to 0.46 logMAR, with two eyes showing PL, two eyes detecting HM, and one eye CF (P = 0.0002); at the last review, mean VA score was 0.36 logMAR, with three eyes showing PL and four eyes detecting HM (P = 0.0008). Mean pre-operative VA in the type 1 group was 0.47 logMAR, with one eye showing PL, one eye detecting HM, and two eyes CF. At the 2-week post-operative visit, the mean VA had improved to 0.37 logMAR, with one eye showing PL (P = 0.002), and at the latest review, the mean VA was 0.20 logMAR (P = 0.027).

*Conclusion* Our study shows that type 2 DM patients can observe improvement in VA and

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stabilisation of their proliferative retinopathy after early vitrectomy and endolaser for vitreous haemorrahage, which is maintained after long-term follow-up.

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*Keywords:* vitreous haemorrhage; vitrectomy; endolaser

#### Introduction

Diabetic retinopathy (DR) is the leading cause of blindness in the working population in the western world.<sup>1,2</sup> Proliferative DR is characterised by new vessel formation in the retina and optic disc as a result of hypoxia, microangiopathy, and capillary occlusion.<sup>3,4</sup> Vascular endothelial growth factor appears to have a vital role in the pathogenesis of proliferative DR,<sup>5</sup> whereas advanced glycation end products modify the vitreous properties.<sup>6</sup> The new vessels are often adherent to the posterior hyaloid face, with subsequent traction that can lead to vitreous haemorrhage (VH) and/or tractional retinal detachment.<sup>7</sup>

The visual outcome after early vitrectomy in type 1 diabetics is well established: The Diabetic Retinopathy Vitrectomy study (DRVS)<sup>8,9</sup> for severe VH examined 616 eyes with VH reducing visual acuity (VA) to 5/200 or less and had a VH for a least 1 month, with surgery carried out within 6 months of VH. They reported improved VA at both the 2-year and 4-year follow-up in type 1 diabetics compared with the <sup>1</sup>Department of Ophthalmology, Royal Berkshire Hospital, Berkshire, UK

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deferral group. However, this benefit was not mirrored in the type 2 diabetics.

With further advances in vitrectomy techniques and instrumentation,<sup>10–13</sup> as well as the advent of endolaser,<sup>14–17</sup> the visual outcome of a type 1 diabetic patient improved further.<sup>18</sup>

The literature suggests that only type 1 diabetics benefit from early vitrectomy and endolaser. We present the result of long-term visual outcomes in a predominantly type 2 diabetic population, with VH and no evidence of tractional retinal detachment affecting the macula.

## Materials and methods

A retrospective review of the case notes of 88 eyes of 80 patients who had vitrectomy and endolaser within 6 months of VH for proliferative DR was carried out. All operations were carried out by a single surgeon (LB) between 2000 and 2007, with at least 2 years of follow-up (range 24–100 months, mean 44 months).

## Study population

In all, 69 eyes of 62 patients were type 2 diabetics and the remaining 19 eyes of 18 patients were type 1 diabetics.

# Data collected

General patient demographics such as age and gender were recorded, as well as type, duration, and classification of DR, both pre- and post-operatively. Pre-operative, post-operative, and most recent VA, laser burns before and at surgery were also compared. Any operative complications were noted.

# **Operative** procedure

All patients underwent a 20-gauge three-port pars plana vitrectomy, removing blood and vitreous from the anterior to posterior vitreous face with a suction cutter probe.<sup>9</sup> Fibrovascular membranes were removed by delamination and/or segmentation, as appropriate. Green-scatter endophotocoagulation was applied to fill in areas of untreated retina. Fluid/air exchange was performed if retinal holes were found or caused during surgery, and if the patient was postured appropriately.

# Results

The mean age of the 62 type 2 diabetic patients was 63.1 years, with an average duration of diabetes of 18.4 years before vitrectomy. In the type 1 population, the average age was 47.9 years with the duration of diabetes before

surgery being 25.7 years. The male/female ratio was 48:21 in the type 2 group and 10:9 in the type 1 group. In the type 2 group, diabetes was controlled with insulin in 44 patients, tablets in 23 patients, and diet only in 2 patients.

# Laser burns

All patients had proliferative DR with VH, and underwent surgery within 6 months, as recommended by the DRVS. The mean numbers of laser burns before surgery were 1865 and 2431 in the type 2 and type 1 population, respectively. The mean operative endolaser burns were 580 and 552 in the type 2 and type 1 populations, respectively.

# VA

Mean pre-operative VA in the type 2 group was 0.64 logMAR, with one eye showing perception of light (PL), 10 eyes detecting hand movements (HMs), and seven eyes counting fingers (CFs). At the 2-week post-operative visit, the mean VA had improved to 0.46 logMAR, with 2 eyes showing PL, 2 eyes detecting HM, and 1 eye CF. At the most recent clinical appointment, the mean VA score was 0.36 logMAR, with three eyes showing PL and four eyes detecting HM (Table 1). The improvement in VA at post-operative review as well as at the most recent clinical appointment was statistically significant: P = 0.0002 and P = 0.0008, respectively.

Mean pre-operative VA in the type 1 group was 0.47 logMAR, with one eye showing PL, one eye detecting HM, and two eyes CF. At the 2-week post-operative visit, the mean VA had improved to 0.37 logMAR, with one eye showing PL. At the most recent clinical appointment, the mean VA was 0.20 logMAR (Table 1). Again, the improvement in VA at the post-operative review as well as at the most recent clinical appointment was statistically significant: P = 0.002 and P = 0.027, respectively.

**Table 1** Pre-operative, post-operative and latest visual acuityin both type 1 and type 2 groups

	Pre-operative VA		Post-operative VA		Final VA	
	Type 2	Type 1	Type 2	Type 1	Type 2	Type 1
LogMAR	0.64	0.47	0.46	0.37	0.36	0.20
NPL	0	0	0	0	0	0
PL	1	1	2	1	3	0
HM	10	1	2	0	4	0
CF	7	2	1	0	0	0

# Retinopathy classification

All patients pre-operatively had active proliferative disease and some (see below) showed evidence of tractional retinal detachment (macular sparing). The final retinopathy grading of the type 2 population showed only one eye with active proliferative disease and with the other 68 eyes graded as treated (currently inactive) proliferative DR. A total of two patients had clinically significant macular oedema and one patient had ischaemic maculopathy. In the type 1 group, none of the patients was proliferating at their last clinical appointment, and one patient had clinically significant macular oedema.

## Intra-operative complications

There were no intra-operative complications; however, six eyes (8.7%) of the type 2 group and three eyes (15.8%) of the type 1 group had non-macular tractional retinal detachment discovered at the time of surgery. None of these progressed to involve the macula, and at the final follow-up visit, three eyes (4.3%) in the type 2 group and no eyes in the type 1 group showed evidence of localised non-macular tractional retinal detachment.

Follow-up ranged from 24 to 100 months, with no patients lost during follow-up.

## Comparison with DRVS

The criteria for patients in the DRVS included vitrectomy within 6 months, VA between 5/200 to light perception. Using the same criteria, 24 eyes of 21 patients with type 2 DM and nine eyes of seven patients with type 1 DM were identified. The VA outcomes after 2 years were compared with the DRVS 2-year follow-up<sup>7</sup> (in which endolaser was not used) as well as with the study conducted by Chaudhry *et al*<sup>18</sup> (in which endolaser was used) (Table 2).

In the type 2 DM group, the pre-operative VA score was an average of 1.6 logMAR in 5 eyes, CF in 6, HM in 12, and PL in 1. At the 2-week post-operative visit, the VA score had improved to 0.60 logMAR, with two eyes showing PL. At the most recent clinical appointment, the VA scores improved to 0.36 logMAR, with two eyes showing PL and one eye detecting HM.

In the smaller type 1 DM group, the pre-operative VA was CF in six eyes, HM in one, and PL in two. At the 2-week post-operative visit, the VA had improved to 0.63 logMAR, with two eyes detecting HM and one eye showing PL. At the most recent clinical appointment, the VA scores improved to 0.48 logMAR, with one eye showing PL.

Table 2	Comparison	of final	VA at 2	2-year period
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	Cumulative %				
	Type 2 DM (our study)	Type 1 DM (our study)	DRVS	Type 1 DM with endolaser	
6/6	12.5	33.3	7.5	25.0	
6/12	58.3	66.7	24.5	58.3	
6/60	83.3	66.7	53.8	91.6	
HM	91.7	88.9	70.8	100	
PL	100	100	75.1	100	
NPL	100	100	100	100	

Comparing the results directly with the DRVS, 58.3% of type 2 and 66.7% of type 1 DM patients achieved VA equal to or better than 6/12, compared with 24.5% in the DRVS. These cumulative figures for VA equal to or better than 6/60 were 83.3 and 66.7% for the type 2 and type 1 DM groups, respectively, compared with 53.8% in DRVS.

### Discussion

The majority of patients with proliferative DR are treated successfully with panretinal photocoagulation.<sup>19–21</sup> Numerous studies including the DRVS<sup>8,9</sup> have clearly demonstrated the advantage of early surgical intervention in the more severe cases in the type 1 DM population. Adjuvant endolaser has been shown to further improve long-term visual outcome.<sup>18</sup> There is no evidence, however, to suggest that this benefit is obtained in the type 2 DM population. The improved visual outcomes in type 1 DM population was speculatively put down to better macula function, less development of lens opacity, and lesser susceptibility to untoward events.<sup>8</sup> It was also suggested that the younger type 1 DM patients had greater severity of new vessels, fibrous proliferations, and vitreoretinal adhesions.

It is broadly accepted now that leaving a VH *in situ* while retinopathy may continue unobserved is unacceptable, and that early vitrectomy in a non-clearing VH is useful for not only clearing the visual media but also allows retinal observation and may stabilise the retinopathy.

Our study shows that type 2 DM patients can obtain sustained improvement in VA and stabilisation of their proliferative retinopathy after early vitrectomy and endolaser that is comparable to the type 1 population, a finding that was not mirrored in the DRVS. The reason for this difference is likely to be mutifactorial; earlier intervention, better instrumentation, adjuvant operative endolaser, and panretinal photocoagulation before VH are all likely to have a role in better long-term outcomes with regard to VA, as well as retinopathy classification, compared with the DRVS population. It would be interesting to observe whether this improvement is more pronounced with small-gauge vitrectomy, and whether the visual recovery is more rapid compared with the 20-gauge vitrectomy in our population.

Clearly, each patient's particular situation and disease state must be carefully considered; however, there is growing evidence that early vitrectomy for VH, in the absence of tractional retinal detachment affecting the macula, has a beneficial effect of long-term visual outcomes in proliferative retinopathy.

#### Summary

#### What was known before

• Early vitrectomy for vitreous haemorrhage is not beneficial in type 2 diabetics.

#### What this study adds

• Early vitrectomy for vitreous haemorrhage is beneficial in type 2 diabetics with regards to visual acuity and stabilisation of their proliferative retinopathy.

#### **Conflict of interest**

The authors declare no conflict of interest.

#### References

- 1 Klein R. The epidemiology of diabetic retinopathy: findings from the Wisconsin epidemiological study of diabetic retinopathy. *Int Ophthalmol Clin* 1987; **27**: 230–238.
- 2 Congdon N, O'Colmain B, Klaver CC, Klein R, Muñoz B, Friedman DS, *et al.* Eye Diseases Prevalence Research Group. Causes and prevalence of visual impairment among adults in the United States. *Arch Ophthalmol* 2004; **122**: 477–485.
- 3 Fong DS, Ferris FL, Aiello LO, Klein R. Diabetic retinopathy. *Diabetes Care* 2004; **27**: 2540–2553.
- 4 Joussen A, Smyth N, Niessen C. Pathophysiology of diabetic macular edema. Dev Ophthalmol 2007; 39: 1–12.
- 5 Adamis AP, Shima DT. The role of vascular endothelial growth factor in ocular health and disease. *Retina* 2005; **25**: 111–118.
- 6 Dodson PM. Management of diabetic retinopathy; could lipid-lowering be a worthwhile modality? *Eye* 2009; **23**: 997–1003.

- 7 Takahashi M, Trempe CL, Maguire K, McMeel JW. Vitreoretinal relationship in diabetic retinopathy. A biomicroscopic evaluation. Arch Ophthalmol 1981; 99: 241–245.
- 8 The Diabetic Retinopathy Vitrectomy Study Research Group. Early vitrectomy for severe vitreous hemorrhage in diabetic retinopathy. Two year results of randomized trial. Diabetic Retinopathy Vitrectomy Study report 2. Arch Ophthalmol 1985; 103: 1644–1652.
- 9 The Diabetic Retinopathy Vitrectomy Study Research Group. Early vitrectomy for severe vitreous hemorrhage in diabetic retinopathy. Four year results of randomized trial. Diabetic Retinopathy Vitrectomy Study report 5. Arch Ophthalmol 1990; 108: 958–964.
- 10 Aaberg TM, Abrams GW. Changing indications and technique for vitrectomy in management of complications of diabetic retinopathy. *Ophthalmology* 1987; **94**: 775–779.
- 11 Machemer R, Hickingbotham D. The tree-port microcannular system for closed vitrectomy. Am J Ophthalmol 1985; 100: 590–592.
- 12 De Bustros S, Thompson JT, Michels RG, Rice TA. Vitrectomy for progressive proliferative diabetic retinopathy. *Arch Ophthalmol* 1987; **105**: 196–199.
- 13 Thompson JT, Glaser BM, Michels GR, de Bustros S. The use of intravitreal thrombin to control hemorrhage during vitrectomy. *Ophthalmology* 1986; **93**: 279–282.
- 14 Fleischman JA, Swartz M, Dixon JA. Argon laser endophotocoagulation. An intraoperative trans-pars plana technique. Arch Ophthalmol 1981; 99: 1610–1612.
- 15 Landers III MB, Trese MT, Stefansson E, Bessler M. Argon laser intraocular photocoagulation. *Ophthalmology* 1982; 89: 785–788.
- 16 Parke II DW, Aaberg TM. Intraocular argon laser photocoagulation in the management of severe proliferative vitreoretinopathy. *Am J Ophthalmol* 1984; 97: 434–443.
- 17 Liggett PE, Lean JS, Barlow WE, Ryan SJ. Intraoperative argon endophotocoagulation for recurrent vitreous hemorrhage after vitrectomy for diabetic retinopathy. *Am J Ophthalmol* 1987; **103**: 146–149.
- 18 Chaudhry NA, Lim ES, Saito Y, Mieler WF, Liggett PE, Filatov V. Early vitrectomy and endolaser photocoagulation in patients with type 1 diabetes and severe vitreous hemorrhage. *Ophthalmology* 1995; **102**: 1164–1169.
- 19 The Diabetic Retinopathy Study Research Group. Preliminary report on effects of photocoagulation therapy. *Am J Ophthalmol* 1976; **81**: 383–396.
- 20 The Diabetic Retinopathy Study Research Group. Photocoagulation treatment of proliferative diabetic retinopathy: the second report of Diabetic Retinopathy Study findings. *Ophthalmology* 1978; **85**: 82–106.
- 21 The Diabetic Retinopathy Study Research Group. Photocoagulation treatment of proliferative diabetic retinopathy. Clinical application of Diabetic Retinopathy Study (DRS) findings, DRS report number 8. *Ophthalmology* 1981; 88: 583–600.

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# Long-term visual and retinopathy outcomes in a predominately type 2 diabetic patient population undergoing early vitrectomy and endolaser for severe vitreous haemorrhage

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- 1. Which of the following is considered the most important factor in the pathophysiology of proliferative diabetic retinopathy?
  - A Insulin
  - B Glucose
  - C Vascular endothelial growth factor
  - D Anti-mitotic nerve growth factor
- 2. The beneficial visual outcomes of early vitrectomy for severe vitreous haemorrhage (VH), with surgery performed within 1 month of haemorrhage have been well demonstrated for which of the following?
  - A Type 1 diabetes
  - B Type 2 diabetes
  - C Both type 1 and 2 diabetes
  - D Neither type 1 nor type 2 diabetes
- 3. Which of the following patients showed improvement in visual acuity at 2 weeks and at the most recent clinic appointment?
  - A Type 1 diabetes only
  - B Type 2 diabetes only
  - C Both type 1 and 2 diabetes
  - D Neither type 1 nor type 2 diabetes

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- 4. Which of the following best describes the proportion of eyes in patients with type 1 diabetes undergoing vitrectomy and endolaser treatment for VH that showed non-macular tractional retinal detachment at the time of the procedure?
  - A 8%
  - B 16%
  - C 24%
  - D 32%

#### **Activity Evaluation**

1. The activity supported the learning objectives.				
Strongly Disagree	Strongly agree			
1 2	3	4 5		
2. The material was organised clearly for learning to occur.				
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Strongly Disagree		Strongly agree		
1 2	3	4 5		