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Factors predicting visual improvement post pars plana vitrectomy for proliferative diabetic retinopathy

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影响增殖性糖尿病视网膜病变玻璃体切除术后视力改善的因素

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摘要

目的:分析影响增殖性糖尿病视网膜病变(PDR)玻璃体切除术后视力改善的因素。

方法:回顾性分析。收集 2014-01/2014-12 在马来西亚吉打州,亚罗士打 Sultanah Bahiyah 医院收治的 PDR 行玻璃体切除术病例资料,包括 1y 内患者统计,基线视力(VA)和 LogMAR 术后最佳矫正视力。使用 IBM SPSS Statistics Version 22.0 进行数据分析。

结果:共 103 例患者。平均年龄 51.2y。在多变量分析中,每个 0 logMAR 基线 VA 的 1 logMAR 术前正偏差与 0.859 logMAR 的术后改善相关($P<0.001$)。同样,术前附着的黄斑与玻璃体切除术后的 logMAR 视力改善相关($b=0.374$,$P=0.003$)。无虹膜新血管和无术后并发症与玻璃体切除术后改善的 logMAR 视力相关,分别为 1.126($P=0.001$)和 0.377($P=0.005$)。无长效眼内填充与玻璃体切除术后 logMAR 视力改善相关,为 0.302($P=0.010$)。

结论:玻璃体切除术后与视力改善的相关因素是:术前视力较差,黄斑附着,无虹膜新生血管,无术后并发症和未使用长效眼内填充物。了解视力改善的因素将有助于玻璃体视网膜手术的决策。

关键词:玻璃体切除术;玻璃体出血;牵引性视网膜脱离;视觉预后;糖尿病性眼病;糖尿病性视网膜病变

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Abstract

• AIM: To identify factors predicting visual improvement post vitrectomy for sequelae of proliferative diabetic retinopathy (PDR).

• METHODS: This was a retrospective analysis of pars plana vitrectomy indicated for sequelae of PDR from Jan. to Dec. 2014 in Hospital Sultanah Bahiyah, Alor Star, Kedah, Malaysia. Data collected included patient demographics, baseline visual acuity (VA) and post-operative logMAR best corrected VA at 1y. Data analysis was performed with IBM SPSS Statistics Version 22.0.

• RESULTS: A total of 103 patients were included. The mean age was 51.2y. On multivariable analysis, each pre-operative positive deviation of 1 logMAR from a baseline VA of 0 logMAR was associated with a post-operative improvement of 0.859 logMAR ($P<0.001$). Likewise, an attached macula pre-operatively was associated with a 0.374 ($P=0.003$) logMAR improvement post vitrectomy. Absence of iris neovascularisation and absence of post-operative complications were associated with a post vitrectomy improvement in logMAR by 1.126 ($P=0.001$) and 0.377 ($P=0.005$) respectively. Absence of long-acting intraocular tamponade was associated with a 0.302 ($P=0.010$) improvement of logMAR post vitrectomy.

• CONCLUSION: Factors associated with visual improvement after vitrectomy are poor pre-operative VA, an attached macula, absence of iris neovascularisation, absence of post-operative complications and abstaining from use of long-acting intraocular tamponade. A thorough understanding of the factors predicting visual improvement will facilitate decision-making in vitreoretinal surgery.

• KEYWORDS: vitrectomy; vitreous hemorrhage; tractional retinal detachment; visual prognosis; diabetic eye disease; diabetic retinopathy
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INTRODUCTION

Over the past three decades, the global prevalence of diabetes has doubled, from 4.7% in 1980 to 8.5% in 2014[1-2]. As these figures increase, the numbers of those

affected by diabetic retinopathy have also increased, with the prevalence of retinopathy estimated to be 35% among diabetic patients[3]. Although proliferative diabetic retinopathy (PDR) forms but a subset of this group, it causes the greatest degree of visual impairment, due to complications like vitreous hemorrhage and tractional retinal detachment.

Since its introduction in 1972, pars plana vitrectomy (PPV) has rapidly become the gold standard of treatment for PDR complications[4-7]. Advances in instrumentation techniques have increased the safety and speed of this procedure[8-11]. However, surgeons face the eternal challenge of balancing the ever-increasing demand for diabetic vitrectomy against the potential visual gain for the patient, especially in the face of limited resources. Kedah is an agricultural state with the highest prevalence of diabetes in Malaysia[12]. This study aimed to determine the factors associated with visual improvement post primary vitrectomy for sequelae of PDR in a tertiary eye centre in Kedah, Malaysia.

SUBJECTS AND METHODS

We conducted a retrospective analysis of all primary PPV indicated for sequelae of PDR from January 2014 to December 2014 in Hospital Sultanah Bahiyah Alor Star, which is the major tertiary eye center serving the state of Kedah and the neighbouring state of Perlis in Malaysia. The data was collected from electronic patient records and hand-written notes documented by the surgeon at the time of surgery. The study was approved by the Medical Research and Ethics Committee, Ministry of Health, Malaysia, and its conduct followed the tenets of the Declaration of Helsinki.

Data collected included patients' demographics, diabetic history (including medications), hypertensive status, indication for PPV, baseline best corrected visual acuity (BCVA) in the operated eye and contralateral eye, post-operative BCVA, use of intra-operative endotamponade, as well as peri-operative complications. Only patients with at least 12mo follow-up were included in the data analysis. Patients with retinal conditions other than diabetic retinopathy were excluded.

Tractional retinal detachment was defined as clinically elevated retina, or if fundus view was obscured, elevated retina detected on ultrasound preoperatively or intraoperatively. Persistent vitreous hemorrhage was defined as non-clearing or recurrent vitreous hemorrhage severe enough to warrant surgery.

A single surgeon performed 23-gauge (G) microincision vitrectomy surgery in all cases, using a high speed vitrectomy machine (Constellation, Alcon USA) and a wide-angle viewing system (EIBOS, Moller-Wedel Germany). In PPV for persistent vitreous hemorrhage, the surgeon would decide on the indication and choice of endotamponade. In cases of tractional retinal detachment with or without a rhegmatogenous component, segmentation and delamination techniques were used to remove fibrovascular membranes. All patients also had intra-operative endolaser.

Table 1 Baseline demographics of patients ($n=93$) at the time of surgery

Characteristics	Frequency(%)
Gender	
M	49 (52.7%)
F	44 (47.3%)
Ethnicity	
Malay	78 (83.9%)
Chinese	10 (10.8%)
Indian	5 (5.4)
Systemic disease	
Hypertension	84 (90.3%)
Ischaemic heart disease	8 (8.6%)
Chronic kidney disease	32 (34.4%)
Cerebrovascular event	2 (2.2%)
Medication for diabetes	
Oral medication	38(40.9%)
Insulin only	29 (31.2%)
Combination therapy (oral and insulin)	24 (25.8%)
None	2 (2.1%)

Data analysis was performed with SPSS 22.0. Visual acuity was converted to logMAR for statistical analysis, with counting fingers, hand movements, perception of light and no light perception being assigned the values 1.85, 2.3, 2.6 and 2.9 respectively. Simple and multiple linear regressions were used to analyze the association between pre-operative characteristics and improvement in visual acuity. Statistical significance was set at $P<0.05$.

RESULTS

Over the period of one year from 1st January 2014 to 31st December 2014, 132 eyes had PPV for complications of PDR. Of these, 29 were excluded because of insufficient duration of follow-up, leaving 103 patients for analysis. Eight patients had bilateral surgery. The mean age was 51.2±9.9y, and the mean duration of diabetes was 9.8±7.3y. All patients had pan-retinal photocoagulation prior to the surgery. Three patients had rubeosis iridis. Other baseline demographic characteristics are summarized in Table 1.

The most common indication for surgery was tractional retinal detachment (50.5%). Endotamponade was used in 39.8% of cases, with silicone oil being the most common endotamponade agent. The mean baseline visual acuity was 1.59+0.7 logMAR, and the mean final visual acuity was 0.91+0.6 logMAR. Other peri-operative details of vitrectomized eyes are outlined in Table 2.

On univariable analysis, the only factors associated with significant improvement in visual acuity at 1y post-vitrectomy were baseline visual acuity in the vitrectomized eye and an attached macula pre-operatively (Table 3). On multivariable analysis, each pre-operative positive deviation of 1 logMAR from a baseline BCVA of 0 logMAR was associated with a

post-operative improvement of 0.859 logMAR ($P<0.001$). Likewise, an attached macula pre-operatively was associated with a 0.374 ($P=0.003$) logMAR improvement post vitrectomy. After adjustment for age, hypertensive status, duration of diabetes, duration of visual loss, and baseline visual acuity in the contralateral eye, the following three features were also found to be associated with visual improvement post vitrectomy; absence of iris neovascularisation, absence of post-operative complications and use of long-acting intraocular tamponade. Absence of iris neovascularisation and absence of post-operative complications were associated with a post-vitrectomy improvement in logMAR by 1.126 ($P=0.001$) and 0.377 ($P=0.005$) respectively. Refraining from the use of long-acting intraocular tamponade was associated with a 0.302 ($P=0.010$) improvement of logMAR post vitrectomy.

Forward multiple linear regression method applied. Model assumptions are fulfilled. There were no interactions among independent variables. No multicollinearity detected. Coefficient of determination (R^2) = 0.615. Final model equation, mean change in logMAR = 2.369 - 0.859 (baseline VA) - 0.374 (macula attached) - 1.126 (no iris neovascularisation) - 0.377 (No complications) + 0.302 (use of long-acting tamponade).

Table 2 Clinical features of vitrectomized eyes $n=103$

Characteristics	Frequency (%)
Indications for vitrectomy	
Vitreous hemorrhage	25 (24.3%)
Vitreous hemorrhage with tractional retinal detachment	7 (6.8%)
Tractional retinal detachment	52 (50.5%)
Tractional retinal detachment with a rhegmatogenous component	19 (18.4%)
Endotamponade	
Nil	62 (60.2%)
Air	3 (2.9%)
Perfluoropropane gas	9 (8.7%)
Silicone oil	29 (28.2%)
Complications	
Intra-operative (lens touch)	2 (1.9%)
Post-operative	
Vitreous hemorrhage	12 (11.7%)
Retinal detachment	6 (5.8%)
Others (macula edema, epiretinal membrane, etc)	6 (5.8%)

DISCUSSION

The growing burden of diabetes is a global phenomenon, with widespread impact on healthcare systems and economic costs[13-17]. Developing countries will feel the strain on their resources most keenly, with a projected increase of 69% in the number of diabetics over the next 15y, as opposed to an increase of 20% in developed countries[16]. The state of Kedah currently has the highest prevalence of undiagnosed diabetes in Malaysia, at 16.1%[12]. Consequently, our diabetic patients tend to present in middle age with end-stage proliferative retinopathy. This has far-reaching consequences for both the patients and their dependents. In these advanced stages, pars-plana vitrectomy is virtually the only means by which these patients may hope to regain functional vision. However, despite continued improvement in visual outcomes post vitrectomy, not all patients will have clinically meaningful visual gains. A utilitarian approach is deemed necessary when selecting cases for vitrectomy, especially as the resources for vitro-retinal surgery are limited. This study identifies five factors which account for approximately 60% of the variance in visual improvement post vitrectomy for sequelae of PDR. Awareness of these will assist the surgeon in counseling patients pre-operatively.

Our study found that absence of pre-operative iris neovascularisation had the greatest effect on improvement in visual acuity post vitrectomy. This finding is in inverse correlation to the results of various other studies, which identified rubeosis iridis as a predictive factor for a poor visual outcome[18-23]. A 10-year study by Thompson *et al*[24] observed that absence of iris neovascularization was associated with a visual acuity of 5/200 or better. However, a more recent study by Ostri *et al*[25] did not find this to be a significant prognostic factor. Iris neovascularisation is stimulated by vascular endothelial growth factor secreted in response to profound retinal ischaemia[26]. We thus postulate that the poor visual outcome associated with rubeosis iridis may be attributed not only to the development of neovascular glaucoma, but also to pre-existing chronic retinal ischaemia. As iris neovascularisation has been observed to be a risk factor for vitreous hemorrhage post diabetic vitrectomy, its absence in an eye planned for vitrectomy may confer a reduced risk of the visual compromise related to this complication[27].

Visual acuity is one of the most objective and easily assessed parameters before vitrectomy. For every 1 logMAR of reduced pre-operative BCVA from a baseline of 0 logMAR (Snellen 6/6), we noted an improvement in the post-operative BCVA by 0.859 logMAR ($P<0.001$). Preoperative visual acuity in the operated eye has been associated with low vision at 3 and 6mo after diabetic vitrectomy[5,25]. As diabetic retinopathy tends to be bilateral and symmetrical, the status of the fellow eye has been regarded as a useful indicator of visual outcome[28]. Yorston *et al*[5] observed that pre-operative vision in the contralateral eye is an independent predictor of poor postoperative vision at 6mo post vitrectomy. Ostri *et al*[25] concurred with these findings, demonstrating that a preoperative visual acuity of <0.1 in the fellow eye was a significant prognostic factor for visual outcome at 1y post vitrectomy. In our study, we emphasize that poor pre-operative visual acuity should not deter surgeons from attempting vitrectomy, as the worse the presenting vision in the operative eye, the greater the post-operative gains observed. Although surgeons are intensely interested in visual

Table 3 Factors associated with change in visual acuity after vitrectomy

Variables	Simple linear regression		Multiple linear regression	
	b[a](95% *CI*)	*P*	b[b](95% *CI*)	*P*
Age	0.005 (−0.012, 0.022)	0.569		
Hypertension	0.062 (−0.628, 0.503)	0.827		
Duration of diabetes	−0.009 (−0.032, 0.015)	0.465		
Duration of visual loss	−0.033 (−0.073, 0.007)	0.107		
Best corrected visual acuity in operated eye	−0.909 (−1.089, −0.729)	<0.001	−0.859 (−1.024, −0.694)	< 0.001
Best corrected visual acuity in other eye	0.026 (−0.214, 0.266)	0.832		
Macula attached	−0.555 (−0.899, 0.210)	0.002	−0.374 (−0.623, −0.126)	0.003
Absence of iris neovascularisation	−0.673 (−1.659, 0.314)	0.179	−1.126 (−1.781, 0.471)	0.001
Absence of post-operative complications	−0.218 (−0.617, 0.182)	0.283	−0.377 (−0.117, −0.637)	0.005
Absence of long-acting intraocular tamponade	−0.337 (−0.678, 0.003)	0.052	−0.302 (−0.530, −0.074)	0.010

[a]Crude regression coefficient; [b]Adjusted regression coefficient.

outcomes as measured by Snellen or logMAR charts, it is important to remember that patients are generally not as interested in their actual visual score as they are in how much functional vision they stand to gain from surgery.

We observed that absence of macula detachment pre-operatively was associated with a 0.374 (P=0.003) logMAR improvement post vitrectomy. A attached macula at baseline has traditionally been associated with a good post-operative outcome[24], and tractional retinal detachment involving the macula has been identified as an independent predictor of poor post-operative visual acuity[5,20,22,29]. The poor vision in these cases is likely due to underlying chronic microvascular insufficiency, as a detached macula loses its source of nourishment from the choroid[29]. This hypothesis is substantiated by a recent study which found macula ischaemia to be a prognostic factor for poor visual outcome in vitrectomies for diabetic tractional macular detachment[30]. Although a previous study has suggested that vitrectomy for tractional retinal detachment is best deferred until the macula is clearly threatened[31], an attached macula clearly confers a greater visual advantage post surgery. The reality in developing countries is that the burden of vitreoretinal surgeries is so great, and the number of qualified surgeons so few, that performing vitrectomy after the macula is detached is the norm. Another obstacle to performing early vitrectomy is that patients generally have relatively good functional vision while the macula is still attached; thus, given their current intact visual acuity, they are often unwilling to undergo surgery just because of the threat of future visual deterioration.

In the current study, absence of post-operative complications was significantly associated with improvement in visual acuity post vitrectomy (P = 0.005). The main post-operative complication in this series was vitreous hemorrhage (11.7%), followed by retinal detachment (5.8%). The rates of post-vitrectomy vitreous hemorrhage vary between studies, from approximately 33% to 60%[32-33]. However, according to Tolentino *et al*[33], this complication does not significantly influence the final visual outcome. Contrarily, Mason *et al*[21] noted that post-operative vitreous hemorrhage is a risk factor for light perception and no light perception vision following diabetic vitrectomy. The main cause of post-vitrectomy diabetic vitreous hemorrhage is residual epiretinal neovascularisation, which is why incomplete scatter photocoagulation before vitrectomy increases the risk[32]. Our rates of post-operative vitreous hemorrhage may have been lower than in other studies due to the fact that all eyes in our study had top-up endolaser intraoperatively. Regarding the effect of intra-operative complications on visual outcome, our study concurred with the results of Ostri *et al*[25], who found no statistical significance of this factor.

Intraocular tamponade plays an important role in vitrectomy; air[34], perfluorocarbon gas[35], and silicone oil[36] have all demonstrated their effectiveness as an adjunct to vitrectomy for their ability to reduce post-operative vitreous hemorrhage. Short-term use of heavy silicone oil has also proven efficacious in improving the anatomic outcome of vitrectomies for complicated retinal detachments and proliferative vitreoretinopathy[37]. We discovered that refraining from the use of long-acting intraocular tamponade was associated with a 0.302 (P = 0.010) improvement of logMAR post vitrectomy. This is in keeping with the results of Ostri *et al*[25], who observed that use of silicone oil for endotamponade is a long-term predictor of low vision after surgery. Likewise, the use of intravitreal gas has also been associated with a poor visual outcome[38]. The association of long-acting intraocular tamponade and poorer vision is likely multifactorial. As discussed above, silicone oil is generally used in more complex cases of proliferative diabetic retinopathy, especially when difficulty with retinal flattening is anticipated, and the risk of retinal re-detachment high. Rates of retinal re-detachment after removal of silicone oil are varied, with up to a quarter of eyes experiencing re-detachment[39-41]. In high risk cases, therefore, surgeons may opt to permanently leave silicone oil in situ, maintaining anatomical retinal integrity with a tradeoff on vision.

One of the strengths of this study is its large cohort of 23-gauge vitrectomies performed by a single surgeon, thus

obviating any effect of inter-surgeon variability of techniques and outcomes. Furthermore, adjustment for confounders was performed during regression analysis to ensure the reliability of our results. However, the authors acknowledge that the study is limited by its retrospective nature, in which data collected from medical records may be influenced by reporting bias. We also did not have sufficient information to evaluate the causes of poor visual outcome, which could have been attributed to the development of cataract or macular ischaemia. We hope to remedy these shortcomings in future, as well as to investigate the potential role of pre-operative anti vascular endothelial growth factor agents, which have been gaining popularity due to their postulated ability to reduce intra-operative bleeding as well as early post-operative vitreous hemorrhage[42-43]. Despite its limitations, our study remains pertinent for its data on the factors associated with visual improvement post diabetic vitrectomy in a South East Asian population.

The mean visual improvement post vitrectomy may be estimated based on the following five factors; poor pre-operative visual acuity, an attached macula, absence of iris neovascularisation, absence of post-operative complications and abstaining from use of long-acting intraocular tamponade. A thorough understanding of the factors predicting visual improvement will not only facilitate decision-making in vitreoretinal surgery, but provide the patient with realistic expectations pre- and post-surgery.

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