Systemic factors influence the prognosis of diabetic macular edema after pars plana vitrectomy with internal limiting membrane peeling

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Abstract

Purpose/Aims: To evaluate the prognostic factors for the best corrected visual acuity (BCVA) and central subfield macular thickness (CSMT) after vitrectomy with internal limiting membrane (ILM) peeling for diabetic macular edema. **Materials and Methods**: A total of 44 eyes of 35 patients who had undergone vitrectomy with ILM peeling between March 2008 and September 2009 were examined. The relationships between preoperative systemic or ocular factors and BCVA or CSMT were evaluated before and at 6 months after the surgical procedure. **Results**: Mean logarithm of the minimum angle of resolution improved from 0.74±0.35 (mean±standard deviation) preoperatively to 0.55±0.4 at 6 months postoperatively (P=0.001). There was a significant improvement of the CSMT from 482±116 μm before the operation to 355±126 μm 6 months after the operation (P<0.0001). The preoperative CSMT was significantly thicker with ischemic disease (P=0.0016). Preoperative BCVA was significantly lower when subfoveal hard exudate was present (P=0.0005). At the 6-month follow-up, CSMT was significantly thicker when there was a higher glycosylated hemoglobin (P=0.008). BCVA at the 6-month follow-up was significantly lower in the group without any diabetes treatment history (P=0.0075) prior to the diagnosis of diabetic retinopathy. **Conclusions**: While BCVA and CSMT were associated with ocular factors before surgery, they were associated with glycemic control postoperatively. Glycemic control may be important for retinal thickness after ocular surgery.

Key words: diabetic macular edema, vitrectomy, glycosylated hemoglobin,

central subfield macular thickness, diabetic retinopathy

Introduction

Diabetic retinopathy (DR) is the leading cause of legal blindness in numerous countries[1]. Complications of DR such as macular edema (ME), vitreous hemorrhage, tractional retinal detachment, or neovascular glaucoma can be present. Diabetic macular edema (DME) is a common cause of visual loss, and is normally treated by focal photocoagulation[2, 3], triamcinolone acetonide[4], and anti-vascular endothelial growth factor[5].

Systemic risk factors for DR have been reported to include glycemic control[6-9], duration of diabetes[8, 9], body mass index (BMI)[9], higher blood pressure[8], and anemia[10, 11]. Systemic risk factors for DME include glycemic control[12], higher blood pressure[12, 13], hyperlipidemia[14], anemia[15], renal disease (proteinuria)[12, 16], and cardiovascular disease[13]. The ocular risk factors for DME have been reported to be advanced retinopathy[13], vitreomacular adhesion[13], and residual internal limiting membrane (ILM) after pars plana vitrectomy (PPV)[17].

PPV is effective for improving ME and visual acuity in some, but not all, cases of DME[17-23]. Several studies have postulated that systemic risk factors are important for the prognosis of DME after PPV[18, 22]. To the best of our knowledge, the specific systemic factors that may be involved have yet to be determined. Therefore, the aim of this study was to evaluate potential prognostic factors for the best corrected visual acuity (BCVA) and central subfield macular thickness (CSMT) after PPV with ILM peeling for DME.

Materials and Methods

This study examined 44 eyes of 35 patients who had undergone PPV with ILM peeling for DME at Nagasaki University between March 2008 and September 2009. We performed PPV with ILM peeling for cases with less than 20/30 on the Snellen scale, diffuse ME of more than 6 months, and suspected thicker posterior hyaloid membrane. None of the patients had undergone panretinal photocoagulation or macular photocoagulation within 3 months before PPV with ILM peeling. In addition, none of the patients had vitreomacular traction syndrome or had received any adjunctive treatment, such as anti-VEGF or triamcinolone acetonide. The CSMT was measured as the central subfield mean thickness by optical coherence tomography (OCT) (Cirrus®, Carl Zeiss Meditec, Dublin, CA). BCVA, fundus examinations, and the CSMT before and at 6 months after the surgeries were retrospectively reviewed using the patients' clinical records.

The relationships between the preoperative systemic or ocular factors and the BCVA or CSMT before and at 6 months after the surgeries were statistically evaluated. The systemic factors examined in our study included age, sex, BMI, systolic blood pressure, hypertension, hyperlipidemia, dialysis, cardiovascular disease, cerebral infarction, no diabetes treatment history until diabetic retinopathy was first found, and preoperative blood test results. A blood test to measure hemoglobin (Hb), hematocrit (Hct), total protein (TP), creatinine, and glycosylated hemoglobin (HbA1c) was performed 1 month before as the standard preoperative assessment and at 6 months after the surgery. The ocular factors examined included epiretinal membrane (ERM), type of macular edema (cystoid or not)[23, 24], proliferative diabetic retinopathy (PDR), panretinal

photocoagulation, focal photocoagulation, and the presence of foveal hard exudates prior to the surgery. BCVA, fundus examination, and optical coherence tomography (OCT) were performed both pre- and postoperatively, with the last tests performed at 6 months after the surgery.

Statistical analysis

Results are expressed as mean±standard deviation. The Mann–Whitney test was used to compare BCVA and foveal average retinal thickness before and after the operation. Multiple regression analysis was used to evaluate BCVA and CSMT, which are related to the above-mentioned systemic and ocular factors. Statistical analysis was performed using StatFlex ver. 5.0 statistical software (Artech Co., Ltd., Osaka, Japan). $P<0.05$ was considered to be statistically significant.

The Ethics Committee of Nagasaki University School of Medicine approved the protocol for this study.

Results

The current study examined 44 eyes of 35 patients (9 females, 24 males; mean age at time of surgery, 62±10 years). Characteristics of the DME patients prior to the surgery are presented in Table 1. The mean logarithm of the minimal angle of resolution was 0.55±0.40 at 6 months after the surgery, which was a significant improvement as compared to the presurgical value of 0.74±0.35 ($P=0.001$) (Figure 1). The CSMT was also significantly improved from a preoperative thickness of 482±116 μm to a thickness of 355±126 μm at 6 months

after the surgery (P<0.0001) (Figure 2). Table 2 shows the relationship between the preoperative systemic or ocular factors and the BCVA or CSMT before and at 6 months after the operation. Preoperative CSMT was significantly thicker with cardiovascular disease or cerebral infarction (P=0.0016). Preoperative BCVA was significantly lower when subfoveal hard exudate was present (P=0.0005). The CSMT was significantly thicker at the 6-month follow-up when there was a higher HbA1c present (P=0.008). The BCVA was also significantly lower at the 6-month follow-up in the group that had no diabetes treatment history until the point when diabetic retinopathy was first found (P=0.0075). Although 24 of the cases underwent indocyanine green staining during the ILM peeling, this was not found to be significantly correlated with either the BCVA or retinal thickness.

Discussion

Similar to previous reports[8,10], the current study also found there was significant improvement of the CSMT and BCVA after PPV with ILM peeling. It has been previously reported that prolonged DME or disruption of the photoreceptor inner/outer segment junction can cause an irreversible visual loss[25]. Thus, these findings suggest that if the surgical intervention for DME is done much earlier and prior to the occurrence of the irreversible visual loss, this could potentially lead to a much better visual acuity prognosis.

Preoperative retinal thickness was thicker in patients with cardiovascular disease or cerebral infarction. The postoperative BCVA was lower in patients with poor glycemic control prior to the surgery, while the postoperative retinal thickness was thicker in patients with higher HbA1c. It has been reported that

recovery was noted in DME patients after either their anemia[10] or serum lipid levels improved[14], or after they were started on dialysis[16]. It has also been reported that cardiovascular disease[13], glycemic control[6-9, 12], and higher BMI[9] are all DR or DME risk factors. Our present results are consistent with these previous findings, as we found both ischemic disease and poor glycemic control were risk factors of DME.

A previous study has reported that the visual acuity was lower when subfoveal hard exudate was present[23]. Similar to these findings, our study also showed that the preoperative BCVA was lower when subfoveal hard exudates were present.

Overall, our results showed there was a correlation between ocular factors such as subfoveal hard exudate and the preoperative BCVA. After the surgery, however, the BCVA and retinal thickness were primarily correlated with systemic factors such as no prior diabetes treatment, and the HbA1c level. Furthermore, the present data also suggest that improvement of the systemic factors is just as important as that seen for the ocular factors.

Interestingly, there were no factors found to be correlated with both the BCVA and the CSMT. However, as previously discussed, BCVA is not always correlated with the CSMT. For example, it has been reported that a poor BCVA was seen with subfoveal hard exudates[23] and that decreased retinal thickness occurred due to foveal atrophy[26].

One of the limitations of the current study included having only a small number of patients. Although it is possible that it is better to simply analyze only one eye per patient, this study included both eyes of 9 patients in the analyses.

Further studies will need to be performed in order to accumulate more cases of DME after PPV with ILM peeling.

In conclusion, BCVA and CSMT were associated preoperatively with ocular factors, while postoperatively they were associated with systemic, but not ocular factors. These changes may be due to improvement of the ocular factors that occur as a direct result of the surgical procedure. Since the BCVA at 6 months after the operation was significantly correlated with no treatment for diabetes prior to the diagnosis of diabetic retinopathy and postoperative glycemic control, better control of diabetes might lead to a better prognosis in DME patients after PPV with ILM peeling.

Declaration of Interests

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Figure Legends

Figure 1. Mean logMAR before and at 6 months after pars plana vitrectomy with internal limiting membrane peeling. The visual acuity significantly improved from 0.74±0.35 (before the operation) to 0.55±0.4 (6 months after the operation) (P=0.001).

logMAR = logarithm of the minimum angle of resolution

Figure 2. Mean central subfield macular thickness before and at 6 months after pars plana vitrectomy with internal limiting membrane peeling. Mean central subfield macular thickness significantly improved from 482±116 μm preoperatively to 355±126 μm at 6 months postoperatively (P<0.0001).

Figure 1.

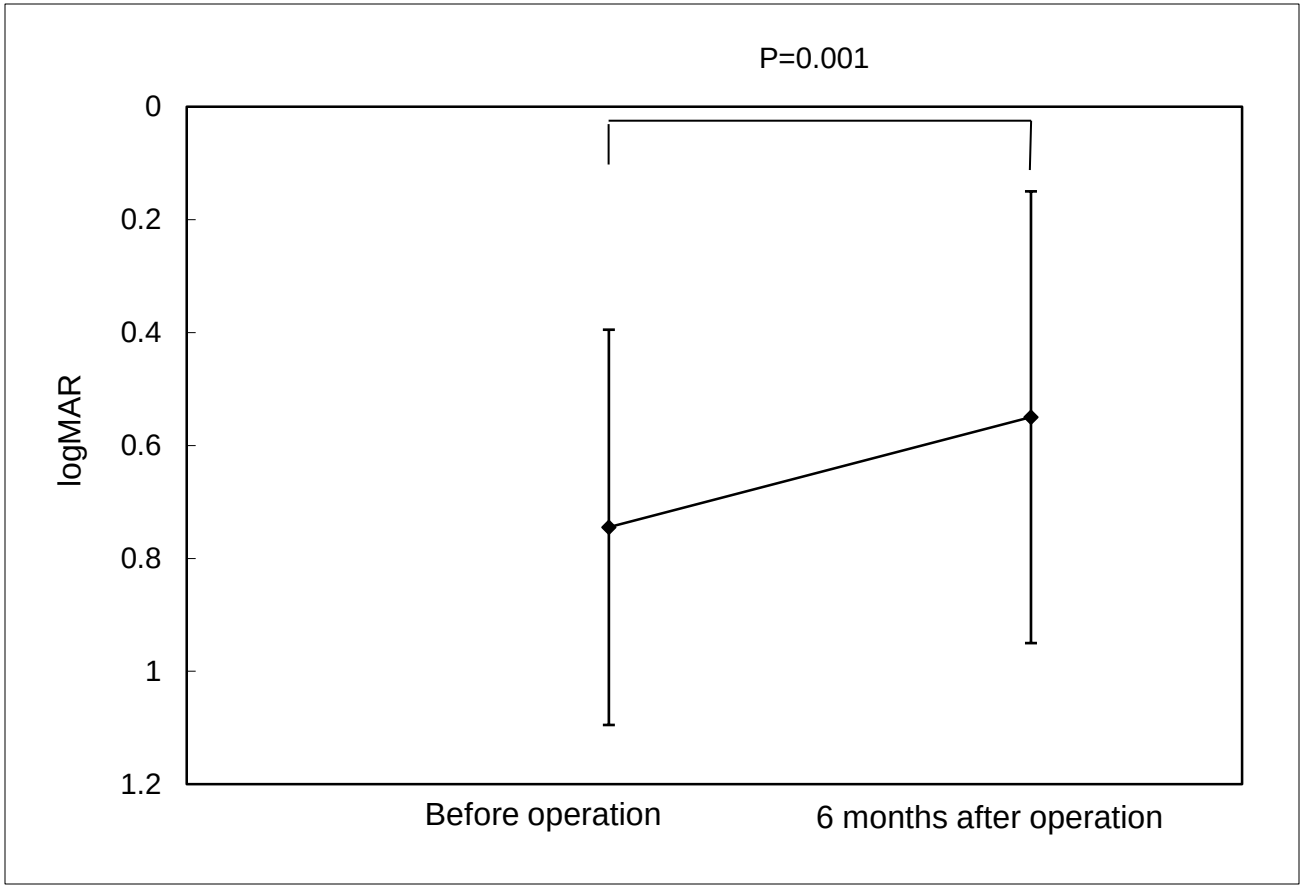
P=0.001
0
0.2
0.4
0.6
0.8
1
1.2
logMAR
Before operation
6 months after operation

Figure 2.

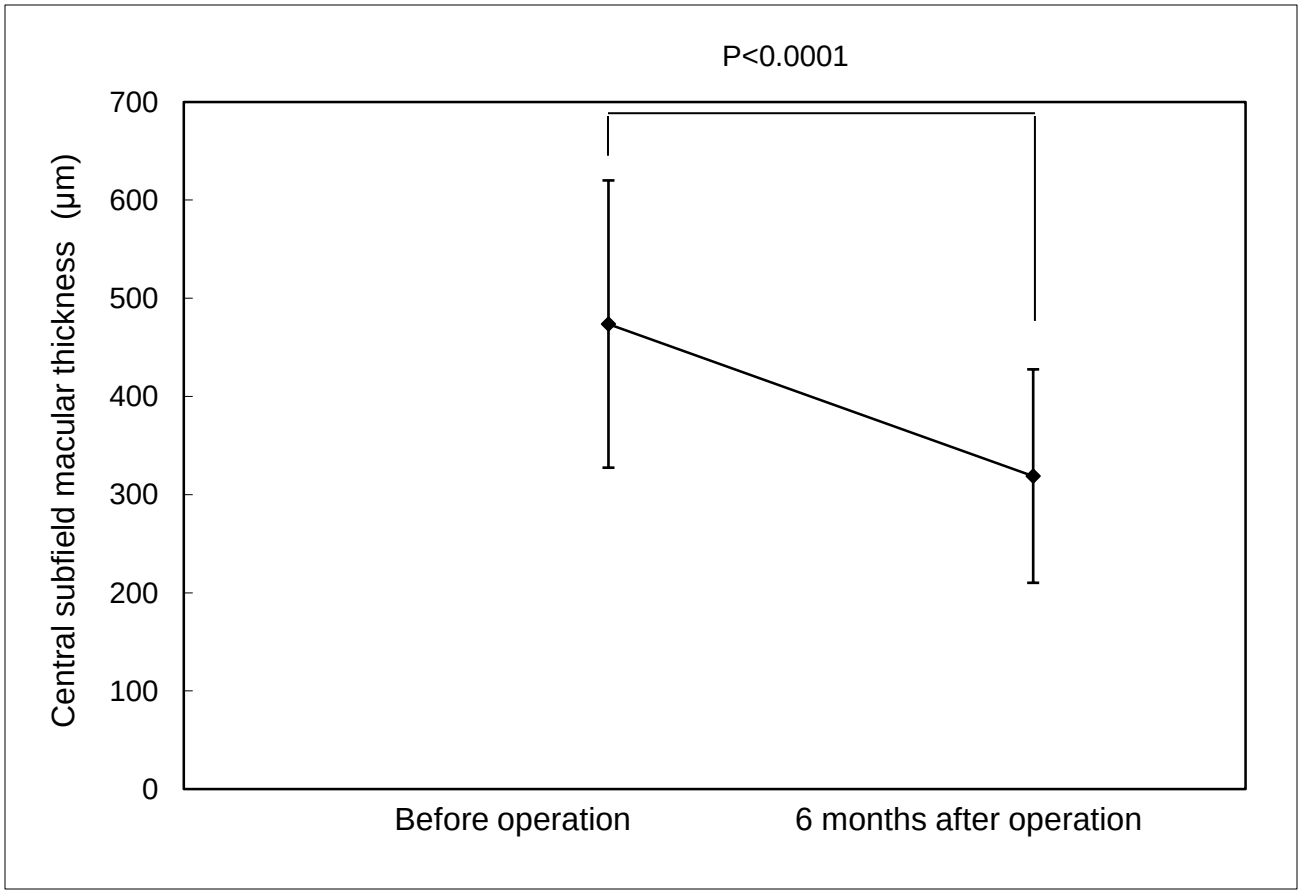
P<0.0001
700
600
500
400
300
200
100
0
Central subfield macular thickness (μm)
Before operation
6 months after operation

TABLE 1. Preoperative characteristics of patients with diabetic macular edema

Systemic factors	**Demographics**		
	Age (years) (mean±SD)	62±10	
	Sex (M:F)	24:9	
	Clinical		
	Body mass index (kg/m^2) (mean±SD)	23.7±4.1	
	Systolic blood pressure (mmHg) (mean±SD)	140±20	
	Hypertension	20	
	Hyperlipidemia	14	
	Dialysis	4	
	Cardiovascular disease or cerebral infarction	4	
	No treatment for diabetes	13	
	Duration of diabetes (years) (mean±SD)	12±9	
	Blood test results (mean±SD) (normal range in Japanese)	Before surgery	6 months after surgery
	Hemoglobin (g/dl) (11.3-15.2)	12.6±1.5	12.4±1.6
	Hematocrit (%) (33.4-44.9)	37.8±4.5	37.3±4.6
	Total protein (g/dl) (6.7-8.3)	7.0±0.6	6.8±0.6
	Creatinine (mg/dl) (0.4-1.1)	1.34±1.61	1.82±2.5
	HbA1c (%) (4.3-5.8)	6.7±0.98	6.7±1.27
Ocular factors (No. of eyes)	Epiretinal membrane	9	
	Cystoid macular edema	14	
	Proliferative diabetic retinopathy	11	
	Foveal hard exudates	6	
	Cataract	32	
	History of PRP	43	
	History of focal photocoagulation	4	

SD = standard deviation

HbA1c = glycosylated hemoglobin

No treatment for diabetes = No history of treatment for diabetes until diabetic retinopathy was found

PRP = panretinal photocoagulation

TABLE 2. Relationships between best corrected visual acuity and foveal average retinal thickness and systemic or ocular factors before and after operation

	Dependent factors	Independent factors	Multiple correlation coefficient (R)	Regression coefficient	P
Before operation	BCVA	Subfoveal hard exudates	0.672	0.580	0.0005
		Creatinine		0.06	0.014
	Retinal thickness	Cardiovascular disease or cerebral infarction	0.580	183.092	0.0016
		Systolic blood pressure		-1.810	0.018
After operation	BCVA	No treatment for diabetes	0.583	0.284	0.0075
		HbA1c at 6 months after surgery		-0.119	0.013
	Retinal thickness	Difference of HbA1c before and after operation	0.487	-49.604	0.008
		Cystoid macular edema		37.56	0.09

BCVA = best corrected visual acuity

No treatment for diabetes = No history of treatment for diabetes until diabetic retinopathy was found

HbA1c = glycosylated hemoglobin