Effect of Diabetes Mellitus and Systemic Hypertension on Macular Hole Surgery

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ABSTRACT

Objective: To evaluate the anatomical and functional results of macular hole surgery in patients with diabetes mellitus (DM) and hypertension (HT) without retinopathy.

Study Design: Descriptive comparative study.

Place and Duration of Study: Department of Ophthalmology, Health Sciences University Haydarpaşa Numune Training and Research Hospital, Turkey between January 2016 and December 2020.

Methodology: This study included 141 eyes of 139 patients who underwent pars plana vitrectomy for macular holes. The patients were divided into two groups according to the anatomic closure after surgery. Group 1 (cases) were patients with macular hole closure, and group 2 (controls) were patients whose macular hole was not closed. The patients with and without diabetes mellitus (DM) or hypertension (HT) were compared. All patients did not have retinopathy. After surgery, the anatomical closure rate of the macular hole and the amount of increase in visual acuity were measured. Significance of the difference between the groups was evaluated using chi-square test.

Results: The best-corrected visual acuity (BCVA) was 1.30 logMAR before surgery and 0.7 logMAR after surgery ($p<0.001$). While BCVA was 1.3 logMAR before surgery in the group with DM, it was 0.7 logMAR after surgery ($p<0.001$). In the group with HT, BCVA was 1.3 logMAR before surgery and 0.7 logMAR after surgery ($p<0.001$). The anatomic success rate after surgery in patients with DM was similar to the group without DM ($p=0.93$). The anatomic success rate after surgery in patients with HT was similar to the group without HT ($p=0.46$).

Conclusions: In the absence of retinopathy there is no difference between the success rates of the macular hole surgery in patients with or without DM and HT.

Key Words: *Diabetes mellitus, Hypertension, Vitrectomy, Macular hole.*

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INTRODUCTION

A macular hole is a full-thickness retinal defect involving the fovea that affects central visual acuity first reported by Henry Noyes in 1871.[1] Kelly and Wendell showed that macular holes could be successfully closed surgically in 1991.[2] Over the years, advances in surgical techniques, such as peeling of the internal limiting membrane, have resulted in higher rates of anatomical closure of macular holes.[3] Diabetes mellitus (DM) is a multisystem disease that occurs as a result of the absence, insufficiency, or inability to use the insulin hormone by tissues.

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Diabetic retinopathy, one of the most important complications of this disease, is a leading cause of vision loss today. Prolonged hyperglycemia results in vascular endothelial damage.[4] Also, retinal blood flow and retinal oxygen demand increase with hyperglycemia.[5] Studies have shown some changes in retinal structures such as decreased ganglion cell complex (GCC) layer thickness, and retinal nerve fiber layer (RNFL) thickness loss, and decreased capillary density in patients without clinically determined retinopathy.[6]

Systemic hypertension (HT) is a preventable cause of cardiovascular diseases. Systemic HT may be an important risk factor for various ophthalmological diseases such as hypertensive retinopathy, retinal vascular occlusion, and ocular ischemic syndrome.[7] HT changes both the structure and functioning of small vessels and leads to a decrease in the density of retinal capillaries, which can impair blood flow in the tissue.[8]

Optical coherence tomography (OCT) provided better recognition of macular holes and better evaluation of foveal structures. Recent studies have determined that posterior vitreous detachment (PVD), which causes anteroposterior vitreomacular traction, is responsible for the formation of macular holes.[9-12]

The pathophysiology of macular holes is better understood with optical coherence tomography (OCT). The success rates of macular hole surgeries have gradually increased with the developments in surgical techniques, from the use of tampons to staining the inner limiting membrane with special dyes. Prognostic factors have been investigated to predict the success of macular hole surgery. The size and stage of macular hole, duration of symptoms, and preoperative visual acuity have been reported as preoperative factors so far.[13]

In this study, the aim was to investigate whether macular hole surgery performed in patients with DM and HT but without retinopathy has any effect on anatomical closure and visual recovery.

METHODOLOGY

This is a retrospective, nonrandomized, observational case-control comparative study. The records of patients who underwent pars plana vitrectomy (PPV) for macular hole diagnosis between January 2016 and December 2020 in the ophthalmology clinic of a tertiary hospital were reviewed retrospectively. Ethics committee approval (2021/147-3346 on 17.05.2021) was obtained from the Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee, the study was carried out in accordance with the Helsinki Declaration standards. Patients with full-thickness macular holes who underwent PPV and internal limiting membrane peeling were included in the study. Exclusion criteria were: Patients with retinopathy due to DM or HT, traumatic macular holes, history of vitreous surgery or retinal detachment surgery, high myopia (axial length greater than 26.00 mm or including refractive error greater than - 6.00D), history of uveitis, any fundus disease or history of intravitreal injection, and any ocular pathology other than concomitant visually significant cataract.

A detailed examination of the patients diagnosed with a full-thickness macular hole was performed. Relevant clinical and surgical history information was collected. Spectral-domain optical coherence tomography (SD-OCT) volume scans (Spectralis; Heidelberg Engineering, Heidelberg, Germany) were reviewed at all visits (before macular hole formation, presence of macular hole formation and after vitrectomy). Volume scans consisted of 19 or 25 horizontal B-scans centered on the fovea followed by the previous volume scans with the automatic retina tracking threshold set to 25. The monitoring threshold was kept lower on preoperative OCT images in patients with cataracts.

The SD-OCT definition of full-thickness macular hole (FTMH) was a full-thickness defect in the central fovea that extends from the internal limiting membrane (ILM) to the retinal pigment epithelium (RPE). The best-corrected visual acuity (BCVA) was measured and the anatomical condition of the macula was recorded on OCT. The full-thickness macular hole was defined using the spectral domain OCT criteria used in the International Vitreomacular Traction Study.[14] Optical coherence tomography images obtained before and at the last postoperative visit were reviewed. A minimum of 6 months of postoperative follow-up was required for inclusion in this study. The BCVA values were recorded preoperatively and at the last visit and converted to logarithms of minimum angle resolution (logMAR) acuities.

Patients with DM and HT were compared with patients without DM and HT in terms of anatomical and visual outcomes. After surgery, patients were divided into two types of anatomical results as described by Kang *et al.* İnto type 1 (macular hole is completely closed); and type 2, (macular hole not closed with the absence of the foveal area neurosensory retina).[15] Type 1 closure was considered an anatomical success, while type 2 closure was considered anatomically unsuccessful.

The patients were divided into two groups according to the anatomic closure after surgery. Group 1 included patients with macular hole closure, and group 2 included patients whose macular hole was not closed. In terms of anatomical success and postoperative visual acuity, the patients with DM or HT without retinopathy and patients without DM or HT were compared.

Surgery was performed using a standard 3-port, 23-gauge PPV. When a cataract was present, a combined phacovitrectomy was performed. Twenty three–gauge trocar cannulas were placed 3.5 mm posterior to the limbus. Patients underwent PPV and internal limiting membrane peeling surgery. During surgery, the posterior hyaloid was completely detached from the retina after the core vitrectomy. The brilliant blue injection was applied to visualize the internal limiting membrane in the macular region, the internal limiting membrane was peeled off. Liquid-air exchange was performed and the air in the vitreous cavity was replaced with 20% sulfur hexafluoride or 16% perfluoroethane. After surgery, patients were advised to stay in the prone position for one week.

SPSS (SPSS for Windows, Version 16.0; SPSS, Chicago, IL) program was used for data analysis. Data distribution was analyzed with the Shapiro-Wilk test. General information of the patients was presented. Anatomic closure rates were calculated for macular holes. Demographic variables were expressed as counts and percentages whereas continuous variables were expressed as median and interquartile ranges (IQR). Visual acuity before and after surgery was compared using a *Wilcoxon* signed-rank *test*. The Chi-square test was used between groups to compare anatomical results. Mann-Whitney U-test was used to compare postoperative vision between the two groups. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 141 eyes of 139 patients were included in the study. Of the 139 patients, 82 (58.9%) were female, 57 (41%) were male, and the mean age was 68.7±9 years. The mean age of patients without DM was 68.6 ± 0.9 years, while the mean age of patients with DM was 69.1 ± 1.3 years ($p = 0.97$). The mean age of patients without HT was 67 ± 1.1 years, and the mean age of patients with HT was 70.8 ± 0.8 years ($p = 0.03$). The mean

BCVA was 1.3 (IQR 1.0 - 1.7) logMAR before surgery and 0.7 (IQR 0.7 – 1.3) logMAR after surgery (p<0.001).

In the group with DM, BCVA was 1.3 (IQR 1.0 – 1.7) logMAR before surgery, and final visual acuity after surgery was 0.7 (IQR 0.5 – 1.3) logMAR (p<0.001). While BCVA was 1.3 (IQR 1.0 – 1.7) logMAR before surgery in the group with HT, final visual acuity was 0.7 (IQR 0.5 – 1.3) logMAR after surgery (p<0.001). In patients with DM and HT, BCVA was found to be significantly higher in the post-surgical measurement compared to the pre--surgical measurements (p<0.001, Table I).

Table I: Comparison of patients' best corrected visual acuity (BCVA) before and after surgery.

	Preoperative BCVA	Postoperative BCVA	P*
All patients	1.3 (1.0 – 1.7)	0.7 (0.7 – 1.3)	<.001*
Patients with DM	1.3 (1.0 – 1.7)	0.7 (0.7 – 1.3)	<.001*
Patients with HT	1.3 (1.0 – 1.7)	0.7 (0.7 – 1.3)	<.001*

Variables are presented as median (Q1 – Q3), Wilcoxon signed rank test, p<0.01, DM: Diabetes mellitus, HT: Hypertension.*

Table II: Surgical success in patient groups.

	Patients without DM n (%)	Patients with DM n (%)	P*
Type 1 closure	81 (75%)	25(75.7%)	
Type 2 closure	27 (25%)	8(24.3%)	0.93
	Patients without HT	Patients with HT	
Type 1 closure	56 (72.7%)	50 (78.1%)	P*
Type 2 closure	21 (27.3%)	14 (21.9%)	0.46
Gender			
Male	Patients with DM	Patients without DM	
Type 1 closure	10 (67%)	32 (72.7%)	P*
Type 2 closure	3 (23%)	12 (27.2%)	0.53
Female			
Type 1 closure	15 (75%)	48 (77.4%)	
Type 2 closure	5 (25%)	14 (22.5%)	0.52
Male	Patients with HT	Patients without HT	
Type 1 closure	16 (76.1%)	26 (72.2%)	P*
Type 2 closure	5 (23.8%)	10 (27.7%)	0.74
Female			
Type 1 closure	33(78.5%)	30(75%)	
Type 2 closure	9(21.4%)	10(25%)	0.70
Age (years)			
<65	Patients with HT	Patients without HT	
Type 1 closure	13 (81.2%)	21 (78.7%)	P*
Type 2 closure	3 (18.7%)	6 (22.2%)	0.55
>65			
Type 1 closure	35 (78.7%)	29 (69%)	
Type 2 closure	10 (22.2%)	13 (30.9%)	0.35
<65	Patients with HT	Patients without HT	
Type 1 closure	9 (81.8%)	25 (78.1%)	P*
Type 2 closure	2 (18.1%)	7 (21.8%)	0.58
>65			
Type 1 closure	16 (72.7%)	48 (73.8%)	
Type 2 closure	6 (27.2%)	17 (26.1%)	0.91

Chi-square test, p<0.01, DM: Diabetes mellitus, HT: Hypertension.*

Anatomically, 106 (75.1%) of the surgeries performed on the patients were type 1 closure and 35 (24.9%) of them were type 2 closure. Of the 33 patients with DM, 25 (75.7%) were type 1 closure and 8 (24.3%) were type 2 closure. The anatomical success rate after surgery in patients with DM was similar to the group without DM (p=0.78). Postoperative BCVA was 0.7 logMAR in those without DM and 0.7 logMAR in those with DM (p=0.63). Of 64 patients with HT, 50 (78.1%) were type 1 closure and 14 (21.9%) were Type 2 closure. The anatomic success rate after surgery in patients with HT was similar to the group without HT (p=0.46). Postoperative BCVA was 0.8 logMAR in those without HT, and 0.7 logMAR in those with HT (p=0.36).

No difference was observed between the groups according to age and gender (Table II).

DISCUSSION

In this study, it was found that macular hole surgery was effective in patients with DM and HT. There was no difference in the anatomical and visual results of surgery if retinopathy did not develop due to these diseases. It is not known how these two diseases, which we encounter frequently in our clinical practice, affect the results if retinopathy has not developed. There is no previous study investigating this issue in the literature.

Vascular impairment is considered to be the primary pathophysiological mechanism causing diabetic retinopathy. In recent years, the role of diabetic retinal neurodegeneration (DRN) has become increasingly prominent in the development of diabetic retinopathy and may replace vasculopathy as the primary pathogenic cause of the disease in the future.[16] Functional and structural disorders may have started in the retina of diabetic patients, even if there are no retinal lesions that cannot be detected on examination. Fine microvascular abnormalities may be associated with early functional changes in diabetic patients without retinopathy.[17] Neurovascular damage may develop without retinopathy findings on ophthalmoscopic examination.[18,19] Since DM can affect the retina subclinically, it was investigated whether it has an effect on macular hole surgery in our study. It was found that anatomical and functional success did not differ between patients with DM and patients without DM.

As a result of diabetic neuropathy, which is a common complication in diabetic patients, deterioration of corneal epithelial wound healing and related ocular surface complications can be seen. This condition has been named as diabetic keratopathy.[20] There is no study investigating wound healing after posterior segment surgery in patients with DM. In this study, it was investigated whether this deterioration in wound healing seen in DM patients would affect the results of macular hole surgery, and none was found. However, molecular-based studies are needed to make more precise justifications.

Patients with proliferative diabetic retinopathy may also have a full-thickness macular hole that can be closed surgically. These surgeries are anatomically successful and provide increased vision in patients, but the vision is lower than expected.[21,22]

Disturbances in the neural control of choroidal blood flow occur in various systemic diseases, such as HT and DM, and in these cases may contribute to retinal pathology and dysfunction.[23] OCT angiography study performed in hypertensive patients without hypertensive retinopathy showed that the superficial plexus vessel density was lower and the foveal avascular region enlarged compared to the normal population.[24] Although OCT-A

was not performed in this study, it was found that it did not affect the outcome of macular hole surgery in this study.

Hypertension causes more damage to the nerve fiber layer in patients with diabetes in the absence of retinopathy.[25] In this study, patients with both DM and HT were compared with those and without. There was no difference between the two groups in terms of anatomical and functional outcomes.

The duration of symptoms and the stage of the preoperative macular hole are important prognostic factors for postoperative functional and anatomical outcomes in the surgical success of the macular hole. Therefore, when a full-thickness neuroretinal defect occurs, surgery should be performed as early as possible.[15]

The limitations of this study are that it is a retrospective study. There was no grouping according to the duration of DM and HT. It was not known whether DM and HT were regulated during surgery. In this study, the focus was on the closure of the macular hole on OCT and the increase in visual acuity after surgery. No advanced tests such as visual field, contrast sensitivity, color vision, depth sense, and light adaptation were performed, which evaluate visual function.

CONCLUSION

If there is no clinically determined retinopathy finding in patients with DM and HT, the functional and anatomical results of macular hole surgery do not change. There are reports of lower-than-expected vision in the eyes with retinopathy. Further studies are needed to compare postoperative vision in eyes with retinopathy and eyes without retinopathy.

ETHICAL APPROVAL:
This study protocol was approved by Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (2021/147-3346).

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
YO, NK, MBY: Data collection, and analysis.
YO, RB, AOK: Writing manuscript.
YO, SK: Surgeons.
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