Surgical outcome of full-thickness macular hole secondary to tractional retinal detachment in proliferative diabetic retinopathy

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Purpose: To evaluate the surgical outcome of full-thickness macular hole (FTMH) secondary to active fibrovascular proliferation (FVP) and tractional retinal detachment (TRD) in eyes with proliferative diabetic retinopathy (PDR), and factors influencing the outcome. Methods: This retrospective study included the patients who underwent vitrectomy for FTMH secondary to PDR TRD from 2016 to 2020. Anatomical and visual outcomes were analyzed after six months along with the factors predicting the final outcome and duration of subretinal fluid (SRF) resolution. Results: Group A (macula-off combined RD, i.e., tractional and rhegmatogenous) included 10 eyes, while group B (macula-threatening TRD) included eight eyes. The mean best-corrected visual acuity improved from logMAR 1.21 (Snellen equivalent: 20/324) to logMAR 0.76 (Snellen equivalent: 20/115) (P = 0.008). Seventeen patients gained ≥1 line(s) of vision. Mean visual gain in groups A and B was 3.7 ± 1.9 and 1.9 ± 1.1 lines, respectively (P = 0.051). MH closed in 88.9% eyes. Type 1 anatomical closure was achieved in 88.9% of eyes. At 6 months, SRF and central macular thickness reduced from 479.6 ± 512.5 μm to 11.4 ± 23.5 μm (P = 0.002) and 874.3 ± 422.6 μm to 207.6 ± 81.7 μm (P = 0.0002), respectively. Finally, macular SRF resolved in all the patients. The mean duration for complete SRF resolution was 4.9 ± 3.2 months. Eyes with a shorter duration of diabetes mellitus (rho = −0.49, P = 0.040) and macula-off combined RD (P = 0.048) took a longer time for complete SRF resolution. Conclusion: Good anatomical and visual outcomes can be achieved in eyes with PDR TRD-associated FTMH. The residual macular SRF resolves slowly after the surgery and extra intervention is not required. Macula-off combined RD is associated with worse outcome and a slower SRF resolution rate.

Key words: Combined retinal detachment, fibrovascular proliferation (FVP), full-thickness macular hole (FTMH), proliferative diabetic retinopathy (PDR), tractional retinal detachment (TRD)

Diabetic retinopathy (DR) is one of the leading causes of blindness among the working population.[11] It is associated with various vision-threatening complications such as macular edema, vitreous hemorrhage (VH), tractional retinal detachment (TRD), vitreomacular traction (VMT), and macular hole (MH).[11] MH has been reported in nearly 1.6% eyes undergoing vitrectomy for proliferative DR (PDR).[2] MH in these eyes occurs secondary to the traction produced by active fibrovascular proliferation (FVP) on the foveal edges, which are already weakened by edema and ischemia.[11]

Kelly and Wendel first described vitrectomy and posterior vitreous detachment (PVD) induction as the treatment for idiopathic full-thickness macular hole (FTMH) in 1991.[3] The surgical outcome of idiopathic FTMH has been extensively studied since then.[4] However, many studies have evaluated the outcome of FTMH secondary to active FVP in eyes with PDR TRD.[5-10] Some authors even suggest conservative management for eyes with FTMH and macula attached TRD as the results are not very encouraging.[2,6,7,8] Another controversy related to the management of such eyes is the role of internal limiting membrane (ILM) peeling.[2,8,11,12]

The aim of this study was to evaluate the surgical outcome of FTMH secondary to active FVP and TRD in eyes with PDR. The factors influencing the outcome were also analyzed.

Methods

This retrospective study was done at a tertiary-care ophthalmic institute in south India. Records of all the patients who underwent vitrectomy for FTMH secondary to PDR TRD from 2016 to 2020 were reviewed. The study was conducted after seeking approval from the Institutional Review Board. The study adhered to the tenets of the Declaration of Helsinki. All the patients were explained about the nature of the disease; the available treatment options and associated prognosis and complications. Informed consent was taken from all the patients

An FVP was considered active if new blood vessels were present on its surface and inactive if the vessels were sclerosed.[2] TRD was defined as RD caused by traction produced by the proliferative membranes present over the retinal surface

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Cite this article as: Babu N, Kohli P, Mishra C, Rajan RP, Kumar K, Ramasamy K, et al. Surgical outcome of full-thickness macular hole secondary to tractional retinal detachment in proliferative diabetic retinopathy. Indian J Ophthalmol 2021;69:3302-7.
and/or in the vitreous. Combined RD (tractional and rhegmatogenous) was defined as convex-shaped or bullous RD, in the presence of FVP. Macula-involving TRD was defined as the presence of vitreo-retinal traction along the vascular arcs. Anatomical closure was defined as the flattening or inadequate follow-up (less than 6 months). Neovascular glaucoma, lamellar MH, or MH secondary to patients were excluded in case of prior vitrectomy; presence advised frequent follow-up (at least 6 months). The patients were examined on postoperative day 1, 2 weeks, 1 month, 3 months, and 6 months. The patients were divided into two groups. Group A included patients with FTMH and macula-off combined RD, whereas group B included patients with FTMH and macula-threatening TRD. All the patients underwent a complete ophthalmological examination at pre- and all postoperative visits. The examination included best-corrected visual acuity (BCVA), intraocular pressure (IOP), slit-lamp biomicroscopy, diluted fundus examination, and optical coherence tomography (OCT). BCVA was converted to logarithm of the minimum angle of resolution (logMAR) for statistical analysis. Spectral-domain OCT (Heidelberg Engineering, Heidelberg, Germany) was used to record high-definition raster line scans. The central macular thickness (CMT) was measured using manual caliper, within 1 mm of the macular center. The region with maximum height was considered for further calculations. One end of the caliper was kept at the inner retinal surface or the vitreoretinal interface while the other was kept at the outer retinal surface. The caliper was oriented vertically to avoid oblique measurements.

The patients were operated by one of the three fellowship-trained vitreoretinal surgeons with at least 7-years of post-fellowship experience (NB, RPR, and KK). All the patients underwent 23-gauge pars plana vitrectomy (PPV). Combined phacoemulsification and vitrectomy were performed if the cataract was significant enough to compromise media clarity. Triamcinolone acetonide (Aurocort, Aurolab, India) was used in all the cases to ensure complete removal of the posterior hyaloid. All the fibrovascular membranes were carefully dissected with appropriate use of vitreous cutter and/or microscissors. Care was taken not to create iatrogenic retinotomies. Perfluorocarbon liquid was used to stabilize the retina after all the tractional membranes were completely removed. ILM was stained with 0.05% brilliant blue G (BBG) dye and peeled in a circular fashion for approximately 2DD around the fovea in all the cases. Inverted ILM flap technique was performed in some cases as per the surgeon’s discretion. Internal SRF drainage was done through either a preexisting retinal break or an iatrogenic retinotomy. SRF drainage through the MH was avoided. In case there were no retinal breaks other than the MH, multiple fluid–air exchanges were done over the disc till the MH closed clinically. Endolaser was performed for the skip areas. The type of tamponade (1000 µl silicone oil (SO) or 20% sulfur hexafluoride (SF6)) was decided intra-operatively by the surgeon.

The patients were examined on postoperative day 1, 2 weeks, 1 month, 3 months, and 6 months. The patients were advised frequent follow-ups in case of any complication(s). The patients were excluded in case of prior vitrectomy: presence of neovascular glaucoma, lamellar MH, or MH secondary to pathologies other than DR; unavailability of preoperative OCT; or inadequate follow-up (less than 6 months).

Anatomical and visual outcomes were noted at the end of 6 months. Anatomical closure was defined as the flattening of MH. Type 1 anatomical closure was defined as complete recovery of the neurosensory retina (NSR) over the fovea. Type 2 anatomical closure was defined as incomplete recovery of NSR, leaving the center of the fovea bare. Factors predicting the final visual acuity and rate of subretinal fluid (SRF) resolution were also analyzed. These factors included age, gender, duration of diabetes mellitus (DM), previous panretinal photocoagulation (PRP) or intravitreal injection (IVI), MH size, preoperative CMT and SRF, type of postoperative tamponade, and iatrogenic retinotomy.

Statistical analysis

Statistical analysis was performed by using statistical software STATA 14.1, (Texas, USA). Continuous variables were expressed as mean (± standard deviation) or median (range) and categorical variables were expressed as percentages. Fisher’s exact test was used to assess the association of categorical variables. The student’s t-test/Mann–Whitney U test was used to find out the significant difference of continuous variables between the two study groups. Wilcoxon sign rank test was used to find out the difference between pre- and postoperative visual acuity. Spearman rank correlation was used to find the correlation between various continuous variables and the time required for complete SRF resolution. P < 0.05 was considered statistically significant.

Results

The study included 18 patients (18 eyes), out of which 11 were male and seven were female. The mean age of the patients was 55.7 ± 4.8 years. The average duration of DM was 13.5 ± 6.9 years. Ten patients were being treated with only oral hypoglycaemic agents, while eight required insulin as well. Other systemic diseases included hypertension (n = 12), dyslipidaemia (n = 3), ischemic heart disease (n = 3), and chronic kidney disease (n = 1). Sixteen patients were phakic, while two were pseudophakic. Fifteen patients had undergone prior PRP, while six had undergone prior IVI (6). Ten patients had macula-off combined RD (Group A), while the remaining eight had macula-threatening TRD (Group B) [Fig. 1].

The mean minimum diameter (MD) of MH was 510.8 ± 246.8 µm. The mean preoperative SRF and CMT were 479.6 ± 512.5 µm and 874.3 ± 422.6 µm, respectively. The mean preoperative BCVA was logMAR 1.21 (Snellen equivalent: 20/324). Table 1 shows the comparison of the baseline characteristics in groups A and B.

A combined phacoemulsification-vitrectomy was performed in 12 patients. An inadvertent intraoperative retinotomy was created in seven patients (38.9%). SRF was drained through the preexisting retinal break and/or iatrogenic retinotomy in all the eyes in group A. Inverted ILM flap technique was used in three patients (16.7%). The postoperative tamponading agents used were silicone oil (n = 9, 50.0%) and SF6 gas (n = 9, 50.0%). The proportion of eyes needing a SO tamponade was 70.0% and 25.0% in groups A and B, respectively.

The average follow-up was 16.7 ± 12.1 months (range: 6–48 months). All the patients who received SO tamponade underwent SO removal (SOR) after three months of the primary surgery. The retina was attached in all the patients at the last follow-up. None of the patients required repeat surgery except for SOR and/or cataract surgery. Sixteen patients (88.9%) achieved type 1 anatomical closure, while two patients (11.1%) had type 2 closure [Figs. 2-5]. One eye in each group achieved type 2 closure. The mean postoperative BCVA improved to logMAR 0.76 (Snellen equivalent: 20/115) (P = 0.008). Seventeen patients gained at least 1-line of vision while none of them lost vision. Four (22.2%) patients gained 1-line, three (16.7%) gained 2-lines, four (22.2%) gained 3-lines, three (16.7%) gained 4-lines,
and three (16.7%) patients gained 6-lines of vision. Seven eyes (38.9%) achieved final BCVA ≥20/80. At 6 months, the mean macular SRF and CMT reduced to 11.4 ± 23.5 µm (P = 0.002) and 207.6 ± 81.7 µm (P = 0.0002), respectively [Fig. 6]. Finally, SRF resolved in all the patients without any additional intervention(s). The mean duration for complete SRF resolution was 4.9 ± 3.2 months (range: 1–10 months). Table 1 shows the comparison of the final outcome in groups A and B.

The mean ellipsoid zone (EZ) defect 6 months after the surgery was 747 ± 397.9 µm. The final BCVA did not depend on the length of EZ defect (rho = −0.41, P = 0.089). The eyes with shorter duration of DM (rho = −0.49, P = 0.040) and macula-off...
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Table 1: Comparison of the baseline and postoperative characteristics of the eyes that presented with FTMH secondary to PDR with combined RD and TRD

|                                | Group A FTMH, Macula-off combined RD | Group B FTMH, Macula-threatening TRD | P     |
|--------------------------------|-------------------------------------|--------------------------------------|-------|
| Baseline characteristics       |                                     |                                      |       |
| Number of patients             | 10                                  | 8                                    |       |
| Mean age (years)               | 53.8±5.0                            | 58.0±3.6                             | 0.064*|
| Gender (Male: Female)          | 6:4                                 | 5:3                                  | >0.99 |
| Mean duration of diabetes mellitus (years) | 10.3±5.5                        | 17.5±6.7                             | 0.023*|
| Mean preoperative BCVA         | logMAR 1.54 (Snellen equivalent: 20/693) | logMAR 0.78 (Snellen equivalent: 20/120) |       |
| Mean minimum diameter of FTMH (microns) | 480.4±250.9                      | 548.8±253.1                         | 0.288*|
| Mean pre-operative CMT (microns) | 1634.7±1103.0                   | 526.2±126.3                          | 0.013*|
| Intra- and postoperative characteristics |                                   |                                      |       |
| Tamponading agent used (SO: SF6) | 7:3                                | 2:6                                  | 0.153*|
| Eyes with type 1 anatomical closure | 9/10 (90.0%)                    | 7/8 (87.5%)                          | >0.99 |
| Mean postoperative BCVA (6 months) | logMAR 0.78 (Snellen equivalent: 20/120) | logMAR 0.60 (Snellen equivalent: 20/80) |       |
| Average visual gain            | 3.7±1.9 lines                      | 1.9±1.1 lines                        | 0.051*|
| Postoperative BCVA ≥20/80 (6 months) | 2/10 (20.0%)                | 5/8 (62.5%)                          | 0.145*|
| Postoperative CMT (6 months)   | 219.6±99.0                         | 192.5±56.0                           | 0.501*|
| EZ Defect (6 months)           | 871.6±421.0                        | 592.7±327.5                          | 0.144*|
| Time for SRF resolution        | 6.2±3.6                            | 3.2±1.8                              | 0.048*|

FTMH: Full-thickness macular hole; PDR: Proliferative diabetic retinopathy; TRD: Tractional retinal detachment; BCVA: Best-corrected visual acuity; SO: Silicone oil; SF6: Sulphur hexafluoride; CMT: Central macular thickness; EZ: Ellipsoid Zone; SRF: Subretinal fluid; *in independent t-test; **Fisher’s exact test; †Mann-Whitney U test

![Figure 5: Optical coherence tomography line scans of patient number 3. a) At presentation showing a full-thickness macular hole with macular tractional retinal detachment; b) 15 days post-surgery showing inverted internal limiting membrane flap and resolving subretinal fluid (SRF); c) 1-month and d) 4-month post-surgery showing resolving SRF; and e) 18-month post-surgery showing resolving SRF and ellipsoid zone defect](image)

![Figure 6: Graph showing the resolution of central macular thickness (CMT) and subretinal fluid (SRF) at different intervals after the surgery](image)

combined RD (P = 0.048) took a longer time for complete SRF resolution [Table 2].

Discussion

Idiopathic FTMH usually develops due to tangential and anteroposterior vitreofoveal traction secondary to anomalous PVD. ILM peeling relieves the tangential traction and induces reparative gliosis. The success rate for idiopathic FTMH ranges between 93% and 98%. However, the clinical characteristics and surgical outcomes of secondary FTMH are different. Flynn et al. was the first one to perform a successful vitrectomy for two cases of PDR-associated MH. However, the visual improvement was not encouraging. With advancements in surgical instrumentation and techniques, surgical outcomes have improved. We evaluated the surgical outcome in 18 eyes

Figure 6: Graph showing the resolution of central macular thickness (CMT) and subretinal fluid (SRF) at different intervals after the surgery
with FTMH-associated with TRD. In our series, the patients with macula-off combined RD had a shorter duration of DM, worse BCVA, and greater CMT and SRF. This may be due to the poor metabolic control and/or late diagnosis of DM among these patients. Similar to the previous reports, more than half of the eyes in our series required postoperative tamponade with SO. A higher proportion of eyes with macula-off combined RD required SO tamponade compared to macula-threatening TRD. Similar to that reported in the literature, the anatomical outcome in our study was also cent percent.

The visual outcome reported in the previous studies is highly variable. This is mainly due to the heterogeneous inclusion criteria used by the studies. The visual prognosis was best in the studies that included eyes without FVP and worst in those evaluating combined RD. The outcome of both the groups of our study was comparable to their respective counterparts in the other studies. Table 3 provides a brief comparison of the results of this study vis-a-vis the existing literature.

Yeh et al. reported that the postoperative BCVA depended on the degree of macular elevation. Karimov et al. concluded that the final BCVA depended on the preoperative SRF height and correlated negatively with EZ layer disruption. We also found that the visual outcome was worse in eyes with macula-off combined RD, that is, higher preoperative SRF height. Moreover, the final BCVA correlated negatively with the length of EZ layer disruption. However, the correlation did not reach significant significance.

Karimov et al. reported that macular SRF persisted in these eyes post-surgery and resolved without any intervention in approximately 6.5 months. Similarly, we also found that it took an average of five months for complete resolution of SRF. The reason for persistent SRF in these cases is not completely understood. It has been suggested that the chronic nature of detachment leads to high protein and cellular levels in the SRF, thus increasing its viscosity and slowing the rate of fluid absorption. Karimov et al. found that the preoperative factors could not predict the duration of SRF resolution. However, we observed that the duration of SRF resolution was longer in eyes with a shorter duration of DM and macula-off combined RD. The duration of SRF resolution may have been longer in patients with a shorter duration of DM as the latter mostly presented with macula-off combined RD, which in turn had a slow rate of SRF resolution. We acknowledge that other factors may also have contributed to the rate of resolution, but this could not be identified in this study. Further prospective studies with a larger sample size may help prove or disprove our observations. Some authors have reported that persistent SRF can cause delayed and poor visual recovery. However, additional surgical intervention to drain the SRF should be avoided as it does not affect the final visual outcome.

Table 2: Correlation of the final BCVA and duration for complete SRF resolution with various factors

| Type of tamponadea | BCVA (P) | Duration for complete SRF resolution (P) |
|--------------------|----------|----------------------------------------|
| Gas (85.7%)        | 0.095    | 0.571                                  |
| SO (14.3%)         | 0.756    | 0.485                                  |
| Creation of intraoperative retinotomya | 0.844 | 0.150 |
| Use of inverted ILM flapa | 0.536 | 0.399 |
| Need for systemic insulina | 0.779 | 0.071 |
| Preoperative SRFb   | 0.066    | 0.208                                  |
| Preoperative CMTb   | 0.168    | 0.189                                  |
| Minimum diameter of MHb | 0.373 | 0.905 |
| Duration of DMb     | 0.344    | 0.040                                  |
| Duration for complete SRF resolutionb | 0.608 | NA |

Table 3: Overview of the previous studies evaluating the outcome of FTMH secondary to PDR TRD

| Author               | Number of eyes | Postoperative tamponading agent | Anatomical outcome | Visual outcome |
|----------------------|----------------|---------------------------------|--------------------|----------------|
| Ghoraba[2]           | 8 (Combined RD 5, TRD 3) | Combined RD: 80% SO, 20% gas; TRD: 66.7% SO, 33.3% gas | 87.5%              | Poor (no patient gained BCVA >20/100) |
| Mason et al.[10]     | 6 TRD          | Gas (100%)                      | 100%               | BCVA improved from 20/250 to 20/100. |
|                      |                |                                |                    | BCVA ≥20/70 in 66.7% eyes |
| Yeh et al.[8]        | 23 (Combined RD 6, TRD 17) | SO (52.2%)                           | 82.6%               | BCVA improved from logMAR 1.75±0.18 to 1.43±0.19 |
| Chen et al.[23]      | 10 TRD         | Gas (90%) SO (10%)              | 100%               | BCVA improved from logMAR 1.33±0.39 to 1.02±0.36 |
| Karimov et al.[13]   | 14 TRD         | Gas (85.7%) SO (14.3%)          | 100%               | BCVA improved from logMAR 1.62±0.89 to logMAR 1.0±0.46 |
| Current study        | 18 (Combined macula-off RD 10, macula-threatening TRD 8) | Combined RD: 70% SO, 30% gas; TRD: 25.0% SO, 75.0% gas | 100%               | Macula-off combined RD: BCVA improved from logMAR 1.54 to 0.78; Macula-threatening TRD: BCVA improved from logMAR 0.78 to 0.60 |

FTMH: Full-thickness macular hole; PDR: Proliferative diabetic retinopathy; TRD: Tractional retinal detachment; FU: Follow-up; SO: Silicone oil.
closure rate.\cite{23} As reported by Stewart et al.,\cite{24} more surgeons have now started to peel ILM during diabetic vitrectomy. Chen et al.\cite{25} reported the use of ILM flap for FTMH-associated with TRD. We also used an inverted ILM flap in three cases. Although the rate of SRF resolution was faster in these eyes, this difference was not statistically significant. The final BCVA in these eyes was not better than eyes where only ILM peeling was done.

Many surgeons prefer to perform SRF drainage through the MH itself. However, draining through the MH has been noted to cause retinal pigment epithelium (RPE) damage and adverse functional outcomes.\cite{26} Charles observed that RPE changes occurred in eyes where SRF was drained through the MH and not in eyes where it was drained from other sites.\cite{27,28} He suggested that suction of SRF through the MH causes trauma to the RPE and photoreceptors.\cite{29} Jeon et al.\cite{30} reported that extramacular SRF drainage in eyes with MH-related RD resulted in a better outcome than drainage through the MH. They hypothesized that SRF in such eyes is viscous and its drainage through the MH causes the MH size to increase, thus damaging the surrounding NSR and reducing the closure rate. Similarly, SRF in eyes with diabetic TRD is viscous and the macula is already weak due to the presence of edema and ischemia. Therefore, the thick stream of fluid during SRF drainage can cause mechanical damage to the underlying RPE and photoreceptors as well as the surrounding NSR.\cite{31}

Hence, we preferred to drain the SRF through a preexisting or an iatrogenic retinal break rather than the MH.

The study was limited by its retrospective nature, small sample size, involvement of multiple surgeons, and unavailability of information related to the type of DM and duration of symptoms. However, the rarity of the disease makes it difficult to plan studies with a large sample size. Although multiple surgeons were involved in the study, they were highly experienced in performing diabetic vitrectomy and followed the same surgical protocol. The duration of symptoms and type of DM as prognostic factors could not be evaluated due to the unavailability of data.

**Conclusion**

The results of this study showed that good surgical outcome can be expected in eyes with FTMH secondary to PDR TRD. The outcome in the eyes with macula-off combined RD tends to be worse. Residual macular SRF is seen in most of the eyes post-surgery but resolves without any extra intervention. The rate of resolution is slower in eyes with a shorter duration of DM and macula-off combined RD.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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