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Modified autologous neurosensory retinal transplantation and bevacizumab injection in primary extra-large chronic macular holes

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ABSTRACT

Purpose: To investigate the outcome of primary idiopathic extra-large full-thickness macular holes (FTMH) treated with a modified autologous neurosensory retinal transplantation (ART) adjuncted by bevacizumab (BCZ) injection.

Methods: In this retrospective interventional case series, five consecutive patients with primary extra-large chronic FTMHs were investigated. The ART procedure included internal limiting membrane (ILM) peeling of both donor and macular hole (MH) areas, placement of the harvested tissue under the edges of MH and use of silicone oil tamponade.

Results: The median age was 64 (60–77) years. The first patient developed choroidal neovascularization one month after surgery, which was treated with BCZ injections. Subsequent patients received injection of BCZ (1.25 mg/0.05 mL) into the silicone oil at the end of the initial surgery. At the last follow-up, complete anatomical closure of the MH was achieved in all patients. With the exception of the first patient, all other patients achieved either a final ellipsoid zone (EZ) defect of zero (three cases) or a reduction to 100 μm (one case). The external limiting membrane (ELM) was completely reconstructed in all of patients. All patients demonstrated an improvement in best corrected distant visual acuity (BCDVA) one month after ART surgery, which was sustained throughout the follow-up period (12–42 months). The median LogMAR BCDVA at baseline was 1.4 (1.3–1.4) which decreased to 1.1(1.0–1.1) ($P = 0.041$) at the first month and 1.0 (0.7–1.2) ($P = 0.043$) at the last follow-up.

Conclusions: The use of ART surgery accompanied by BCZ injection appears to be an effective method for primary extra-large chronic FTMHs.

1. Introduction

Surgical management of full-thickness macular holes (FTMH) was first proposed in 1991 by Kelly and Wendel.[1] After that, various surgical repair methods have been used for macular holes (MH)s. In 1997, a study reported that the removal of the internal limiting membrane (ILM) decreased the risk of MH recurrence.[2] Since then, vitreous surgery and ILM peeling have been used as the standard surgical procedure for MH with a closure rate of about 90 %[3,4]; however, in the case of large MH, the chance of closure decreases. In these cases, the inverted ILM flap technique was suggested, which considerably increased the closure rate and improved visual outcome by preventing the postoperative flat-open appearance.[5,6] Other surgical techniques, such as re-vitrectomy with extended ILM peeling in very large MH,[7] autologous free ILM flap transplantation,[8] transplantation of lens capsule,[9] application of sub-retinal fluid,[10] and Superior Wide Base ILM Flap Transposition (SWIFT) have been reported for persistent MHs with previously removed ILM.[11] "Autologous neurosensory retinal free-flap transplantation" (ART) for refractory myopic MH was first suggested by Grewal and Mahmoud.[12] Further studies have reported closure rates ranging from 66.7 % to 100 % and significant improvement in visual function in the short-term follow-up of large refractory or recurrent MHs using the ART technique.[13–20] Moreover, in a long-term follow-up (24 months), good anatomical and functional results were maintained, with a 44 % risk of inner retinal cystic changes but without a significant impairment in visual function.[21] A limited number of studies have reported successful

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outcomes with ART in cases of primary large chronic MHs.[19,22–24] The postoperative closure rate and visual outcome following MH surgeries depends on preoperative MH diameter.[25] Previous reports indicated a lower success rate for conventional MH surgery techniques for MHs with a diameter greater than 400 μm.[26] Moreover, MHs larger than 650 μm have been associated with a poorer prognosis.[27] Multiple surgeries may also increase the risk of retinal trauma and subsequent complications for patients. Therefore, adoption of ART surgery as the primary option for treating primary large chronic MHs, especially those with a hole diameter exceeding 650 μm, is expected to yield improved outcomes for patients. To this end, our study, the first of its kind in Iran, aims to describe the anatomical and functional results of using a partially modified ART surgery to treat patients with primary large chronic idiopathic FTMHs.

2. Materials and methods

This retrospective interventional case series, conducted between November 2019 and June 2022, consecutively recruited patients with primary, extra-large (opening diameter >650 μm or base diameter >1000 μm),[27,28] and chronic idiopathic FTMHs lasting more than 12 months referred to a tertiary referral center in Shiraz, southern Iran. Patients with any previous vitreoretinal surgical treatments, high myopia, retinal detachment, glaucoma, diabetic retinopathy, trauma, or macular degeneration were excluded from the study. This study was conducted in accordance with the Helsinki Declaration and was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1402.059). All patients were informed of the risks and benefits of the surgery, and written informed consent was obtained from each patient prior to the procedure.

Patients were examined both before and after the surgery in terms of best corrected distant visual acuity (BCDVA), which was converted into the logarithm of minimum angle of resolution (LogMAR), intraocular pressure (IOP) measurement, and fundus examination, including fundus photography, binocular indirect ophthalmoscopy, and spectral-domain optical coherence tomography (OCT) imaging. Presence of absolute scotoma in the MH documented by laser beam test (LBT) using Ellex Integro Pro Scan™ laser system (Ellex Medical Pty. Ltd, Mawson Lakes, S.A. 5095, Australia). All patients were followed up for at least 12 months postoperatively.

Anatomical closure rate and graft configuration were assessed using a Spectralis HRA OCT device (Heidelberg Engineering, Heidelberg, Germany). The Ellipsoid Zone (EZ) and External Limiting Membrane (ELM) lines were evaluated before and after surgery, while changes in BCDVA measured using a Snellen chart after surgery, compared to the baseline, were used to assess functional outcomes. To assess the threshold of sensitivity of the grafted tissue to light stimulus, a LBT was performed using the red aiming beam of the laser system. During the LBT, a 100 μm red laser beam was aimed over the grafted tissue, noting the fraction of the maximum possible beam intensity when became visible by the patient as the threshold of light sensation.[29] OCT-angiography (OCT-A) was also performed when feasible.

2.1. Surgical technique

A standard 23-gauge complete 3-port, parsplana vitrectomy (Constellation; Alcon, Fort Worth, Texas) was performed under general anesthesia in all patients. In phakic eyes phacoemulsification and intraocular lens implantation was performed. After staining with MembraneBlue-Dual™ (DORC International, Zuidland, the Netherlands), the ILM surrounding the edge of the MH for approximately one disc diameter, as well as the ILM over an area located in the mid-peripheral retina supratemporal to the vascular arcade, were peeled using end-gripping forceps. The area to be harvested was pretreated with a circular row of laser endophotocoagulation, and a localized detachment was created by injecting balanced salt solution under the retina. The retina graft was harvested and trimmed using intraocular forceps, scissors, and the vitrectomy cutter to approximately 0.5 mm larger than the MH size. The retina around the MH was lifted by microinjection of fluid into the MH, and the graft was gently molded and inserted under the edges of the MH using the technique of low IOP with minimum fluid flow inside the eye during graft manipulation. A soft-tip cannula was used to spread the graft flat. Following placement of additional endolaser barriers around the peripherally made hole, a fluid-air exchange was performed, and silicone oil tamponade was injected. Perfluorocarbon liquids (PFCL), blood, or viscous materials were not used.

Except for the first patient, all patients received an intravitreal injection of bevacizumab (BCZ) (Avastin® F. Hoffmann-La Roch Ltd, Basel, Switzerland) at a dose of 1.25 mg/0.05 mL at the end of the procedure. All surgeries were performed by a single surgeon (H.A.). The silicone oil was removed 6-month after the ART surgery.

2.2. Statistical analysis

Data were analyzed using SPSS statistical software version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as median, range, and frequency. Wilcoxon Signed Ranks Test was used to compare BCDVA values before and after surgery in each patient. A 2-tailed P-value less than 0.05 was considered statistically significant.

3. Results

A total of five eyes of five patients (4 females and one male) with primary extra-large chronic MH underwent the ART procedure. Demographic data, clinical characteristics and anatomical and functional results of surgeries are summarized in Table 1. The median age of patients at the time of surgery was 64 (60–77) years. The median of minimum opening diameter of MHs was 729 (671–823) μm while the median of basal MHs size was 1321 (1176–1543) μm. The median duration of symptom of visual loss was 24 (12–144) months.

Except for patient 2 who was pseudophakic, all other patients were phakic and lens removal by phacoemulsification was done simultaneously. Retinal transplant surgery was performed successfully in all patients without any intraoperative complications. In patient 1, subfoveal choroidal neovascularization (CNV) developed one month after surgery, which was subsequently treated with repeated monthly intravitreal injections of BCZ. The CNV responded to the injections but a subretinal macular scar developed in long term (Fig. 1). As a prophylactic measure, all other patients received an intravitreal injection of BCZ (1.25 mg/0.05 mL) into silicone oil at the end of their initial operation. None of these patients developed CNV during follow-up. The median follow-up time was 12 (range: 12–42) months after the initial ART surgery.

3.1. Anatomical results

Optical coherence tomography images demonstrated complete anatomical closure of MH in all patients (100 %) by six months postoperatively, which was maintained throughout the entire follow-up period (Figs. 1–3). The median preoperative EZ defect was 1485 (1440–2163) μm. Final EZ defect was zero in 3 patients (patients 2 to 4), in patient 5 reduced from 2163 μm to 100 μm. In patient 1, the surgery failed to significantly decrease the EZ defect (from 1461 μm to 1355 μm) due to presence of the CNV scar. The ELM was almost completely reconstructed in the four consecutive patients who received BCZ prophylaxis during surgery and had successful transplantation.

3.2. Functional results

All patients showed improvement in BCDVA one month after ART surgery, which was maintained throughout the follow-up period, except

Table 1
Demographic and clinical characteristics and surgical results of patients with primary large chronic idiopathic macular hole undergoing autologous neurosensory retinal transplantation.

Patient No.	1	2	3	4	5
Age (year)	75	64	64	60	77
Sex	F	F	F	M	F
Eye	OS	OD	OD	OS	OS
Minimum MH Opening Diameter (μm)	823	729	697	671	783
Basal MH Diameter (μm)	1176	1215	1339	1321	1543
Duration of MH (Month)	36	12	15	24	144
Duration of follow-up (month)	42	18	12	12	12
Lens status	phakic (1+ N/S)	pseudophakic	phakic (1+ N/S)	phakic (1+ N/S)	phakic (1+ N/S)
Operation	Phacovitrectomy	vitrectomy	Phacovitrectomy	Phacovitrectomy	Phacovitrectomy
BCDVA (LogMAR)					
Baseline	20/400 (1.3)	20/400 (1.3)	20/500 (1.4)	20/500 (1.4)	20/500 (1.4)
First month	20/250 (1.1)	20/250 (1.1)	20/200 (1.0)	20/200 (1.0)	20/250 (1.1)
Sixth month	20/200 (1.0)	20/200 (1.0)	20/150 (0.875)	20/250 (1.1)	20/100 (0.7)
Final follow-Up	20/320 (1.2)	20/200 (1.0)	20/150 (0.875)	20/200 (1.0)	20/100 (0.7)
EZ defect (μm)					
Pre-op	1461	1485	1440	1920	2163
Final	1355	0	0	0	100
LBT absolute scotoma threshold (Percent of maximum laser beam intensity)					
Pre-op	100	100	100	100	100
Final	100	60	60	50	50

BCDVA = best corrected distant visual acuity; MH = macular hole; LogMAR = logarithm of the minimum angle of resolution; EZ = Ellipsoid Zone; LBT = laser beam test; N/S = nuclear sclerotic cataract.

for patient 1. The median of LogMAR BCDVA at baseline was 1.4 (1.3–1.4) which decreased to 1.1(1.0–1.1) (P = 0.041) at the first month, 1.0 (0.7–1.1) (P = 0.039) at the sixth month, and 1.0 (0.7–1.2) (P = 0.043) at the last follow-up.

Patients 2 through 5 exhibited perception of the laser light targeted over the graft center with a laser beam intensity as low as 50–60 % of the maximum intensity of the aiming beam on LBT after the surgery (Fig. 4A), as opposed to no light perception in the hole, even at 100 % intensity before the surgery.

3.3. Complications

Throughout the follow-up period, there were no postoperative complications such as retinal detachment, flap displacement, epiretinal membrane, or endophthalmitis, except for the case of CNV in the first patient.

4. Discussion

This retrospective case series reports on five patients with primary extra-large chronic idiopathic FTMHs who underwent ART with silicone oil tamponade. Following the occurrence of postoperative CNV in the first patient, intravitreal BCZ was administered prophylactically in the remaining cases. We hypothesized that the anti-angiogenic and anti-inflammatory effects of BCZ would reduce the likelihood of post-operative macular edema (ME) and neovascularization. Complete anatomical MH closure and foveal reconstruction were achieved in all patients, and final visual acuity improved in all patients except the first, which remained close to the baseline. No surgical complications were observed intraoperatively or during the follow-up period in other patients.

Several surgical procedures have been previously proposed for management of primary and refractory large MH including inverted ILM flap, free autologous ILM flap or lens capsule transplantation, arcuate retinotomy, and the use of adjuvants such as autologous blood and platelet-rich plasma. However, the surgical results of these procedures have not been consistent.[5,8,9,30–32]

In 2016, Grewal and Mahmoud described ART for the first time in a case of refractory myopic MH.[12] Since then, different modifications of ART have been used to manage MHs in various situations such as re-fractory, recurrent, or primary MH, myopic MH, and MH-associated retinal detachments.[13–22,24] In a series of seven large chronic MHs, Tanaka et al. harvested the retina under PFCL and positioned it under the MH edges without ILM peeling on either side. They used sulfur-hexafluoride gas as the intraocular tamponade. Five of the re-ported eyes achieved improvement in their visual acuity, one remained unchanged, and one eye deteriorated due to upside-down implantation of the grafted retina. Tanaka et al. also reported an insignificant reduction of EZ defect from 1089 μm to 921 μm (<20 %). Our study demonstrated that the EZ achieved almost complete and continuous alignment in all patients, except for the first patient, which contrasts with the results reported in their study. The reconstitution of the EZ and alignment of neurosensory layers (ANL) on OCT have been described as important prognostic biomarkers associated with better final visual acuity.[19] The lower reduction of EZ defect and absence of continuity of EZ lines in the Tanaka series was probably due to poor ANL between the graft and host retina, as well as edema of the graft in the first few months of their study.[22,24] In another study from the same center, Kitahata et al. reported on 17 eyes with primary large MH undergoing ART. The EZ was reconstructed in 9 patients (52.9 %), and this subgroup demonstrated significantly greater improvement of visual acuity compared to those without restoration of the EZ (P < 0.05). Moreover, the incidence of ME was higher in the group without the EZ. They used the same surgical technique as the Tanaka series but reported a higher rate of EZ resto-ration (52.9 %) consistent with visual acuity improvement, compared to no BCDVA improvement in the EZ-negative subgroup. They reported an overall 17 % ANL in their series.[24]

In our technique, the ILM was peeled in both the donor and recipient sites, followed by the detachment of the macula through microinjection of balanced salt solution into the MH. This facilitated insertion of the graft under the MH. The flap was safely secured under the retina mini-mizing the chance of dislocation or eccentricity during fluid-air ex-change and tamponade injection. PFCL was not used due to the risk of toxicity in ocular tissue[33] and PFCL migration into the subretinal space. Silicone oil was used for prolonged intraocular tamponade and may enhance tissue oxygenation at the graft site.[34,35]

Postoperative imaging demonstrated an anatomically aligned graft (Figs. 2, 3 and 4B). The reconstitution of ELM/EZ suggests integration of transplanted photoreceptors (PRs) with the surrounding PR layer.

ART may have implications for future therapies for other disorders involving the outer retina. It is noteworthy that a new constructed fovea was formed in the central macula of these eyes. CNV has been identified

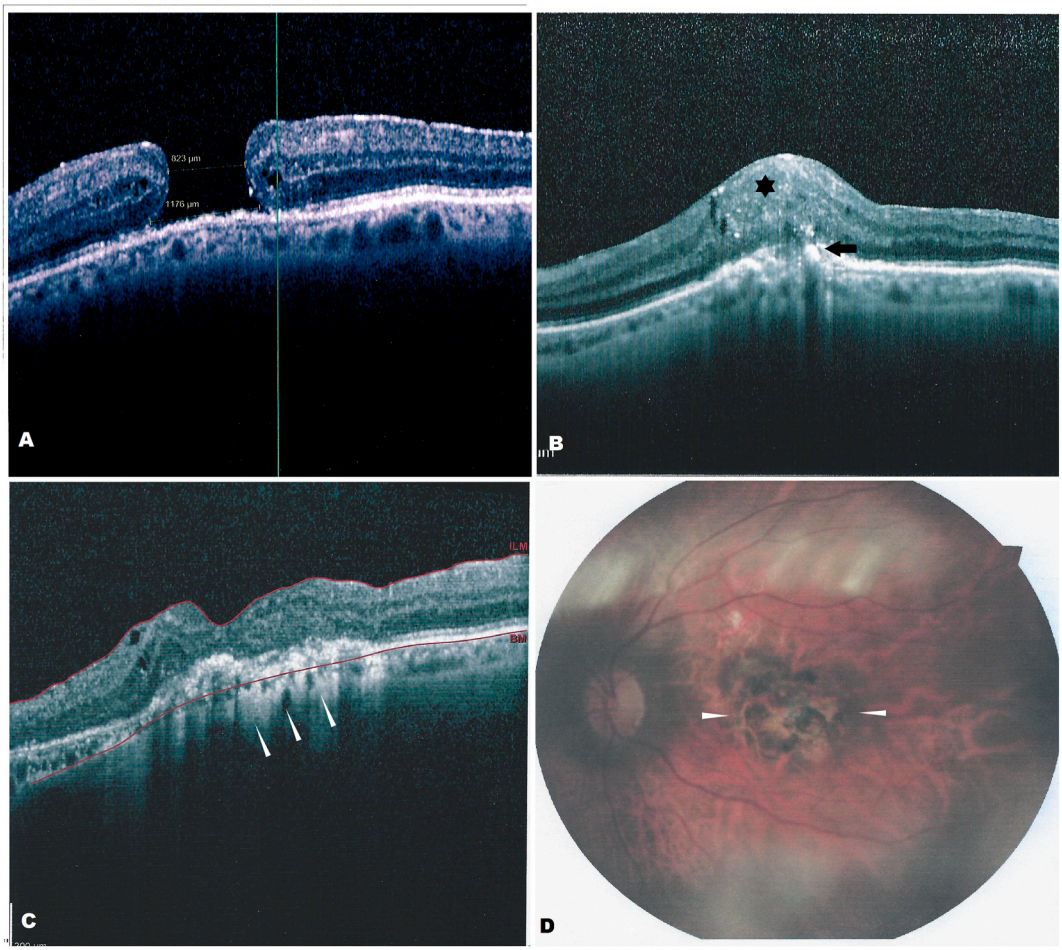

Fig. 1. Patient 1: Baseline and 42 Months after Autologous Retinal Transplant. A: The preoperative optical coherence tomography (OCT) scan revealed a primary, large, and chronic full-thickness macular hole (FTMH) with a basal diameter of 1176 µm (duration of 36 months). The best corrected distant visual acuity (BCDVA) was 20/400. B: The OCT scan taken after the second month of surgery revealed choroidal neovascularization (CNV) (black arrow), which partially responded to the injection of bevacizumab. The inner retina is edematous (asterisk) with somehow disorganized inner layers (DRIL). The BCDVA was 20/250. The optical coherence tomography (C) and color fundus photograph (D) at the 42nd month follow-up showed complete anatomical closure of MH in the presence of a pigmented subretinal macular scar (arrowheads). The BCDVA was 20/320. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

as a rare complication following MH surgery, often resulting in poor visual outcomes. The proposed mechanism was retinal pigment epitheliopathy and defects in Bruch's membrane, whether pre-existing or secondary to surgery as potential predisposing factors for this complication.[36,37] This complication is also reported in the use of human amniotic membrane for MH surgery.[38] The development of CNV in the first patient in our study, as well as in one previous report of ART,[39] led us to incorporate the use of BCZ as an additional therapeutic agent in our technique. The occurrence of CNV in ART surgery may be attributed to the ischemia of the harvested retinal tissue, which may lead to local production of angiogenic factors such as vascular endothelial growth factor (VEGF).[15] Bevacizumab, a VEGF inhibitory agent, selectively targets VEGF-A, which reduces the VEGF protein levels and inhibits the growth of abnormal blood vessels. It decreases vascular leakage and tissue edema. Moreover, by reducing the activity of macrophages and preventing the infiltration of inflammatory mediators, it shows an anti-inflammatory effect that prevents ischemic nerve damage.[40] Anti-VEGF agents have been widely used as an initial treatment for the management of vision loss secondary to diabetic ME involving the center. Because of the effect of BCZ against neovascularization, it has been used to treat ocular neovascularization in age-related macular degeneration, diabetic retinopathy, venous occlusive disorders, and neovascular glaucoma.[41] Successful treatment of myopic CNV has been reported by intravitreal BCZ injection.[42] Anti-VEGF drugs, including BCZ, reduce proliferation and alter the expression of genes related to angiogenesis, apoptosis, inflammation, and oxidative stress in vitro in a variety of retinal cell types such as retinal ganglion cells, Müller cells, RPE cells, and choroidal endothelial cells.[43,44] Tabandeh studied the vascularization of grafted tissue by fluorescein angiography and OCT-A following ART for giant MHs. He reported vascularization and reperfusion of the transplanted retina and hypothesized that the retinal graft produces enough angiogenic stimulus to initiate angiogenesis, resulting in neovascularization and anastomosis between its vascular system and surrounding vascular networks.[15] Using antiVEGF drugs in ART, may hinder vascularization and reperfusion of very large grafts. In our series, the normal superficial foveal vascular contour and partial re-perfusion of the deep vascular plexus of the grafted tissue, as documented in OCT-A (Fig. 4; C to G), is consistent with continued neovascularization and gradual vascular anastomosis between the grafted tissue and the surrounding host retina.

Our study revealed a significant improvement in visual function among all patients, except for the first patient, as evidenced by the positive outcomes of BCDVA and LBT tests, indicating functional activity of the grafted tissue. The mechanism of cross-linking between the grafts and surrounding retina is not well recognized. However, various theories such as Müller cell migration, have been suggested. These

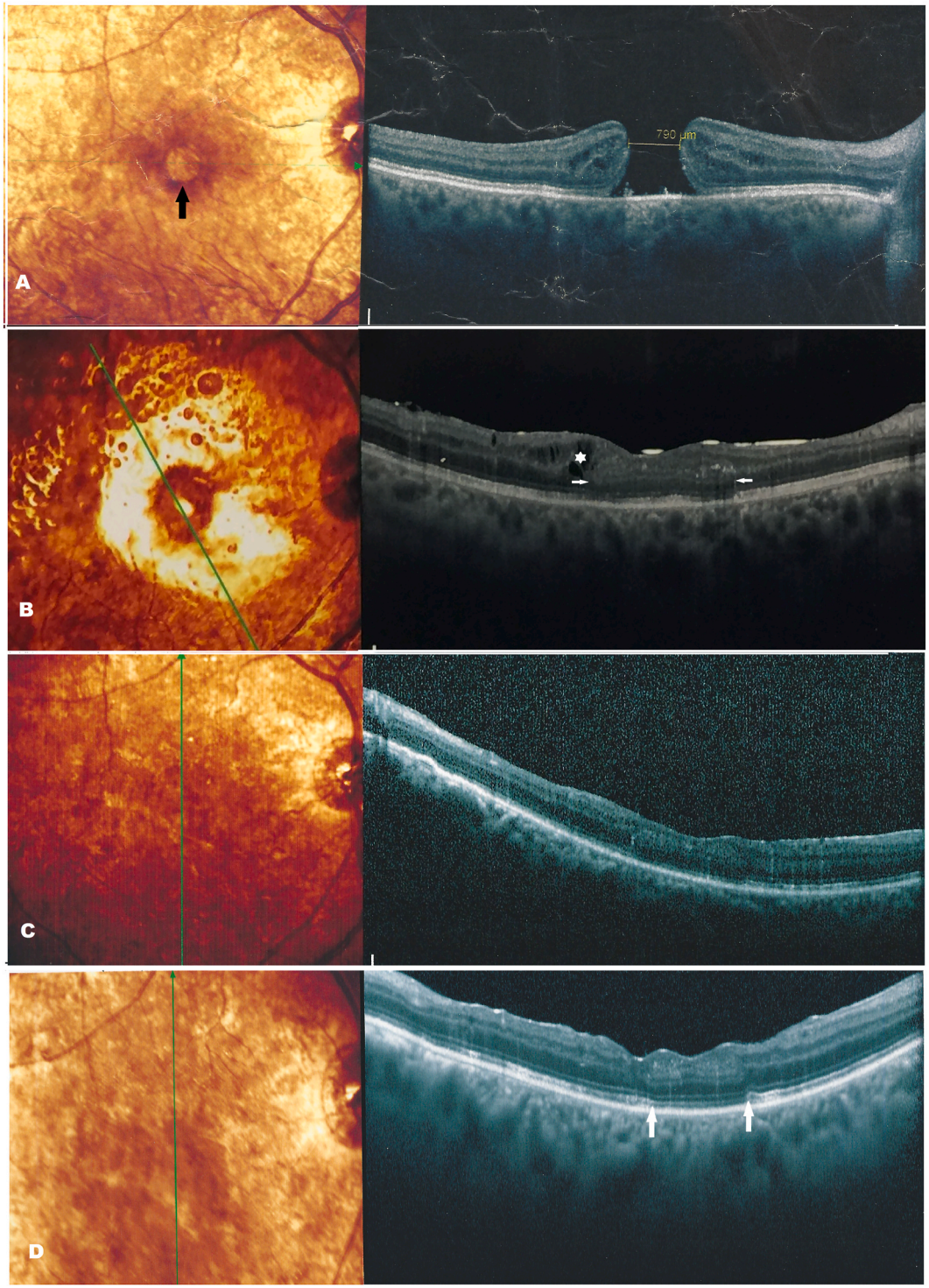

Fig. 2. Optical coherence tomography (OCT) findings after autologous retinal transplantation (ART) of patient 2. A: Preoperative infrared & OCT images showed a chronic macular hole (MH) (black arrow) in the right eye with an opening diameter of 790 µm (duration of 12 months). The best corrected distant visual acuity (BCDVA) was 20/400. B: The OCT scan taken at the fourth month after surgery revealed a silicone-filled eye with a completely closed MH. The grafted neural layers became properly aligned to the recipient site (white arrows), the surrounding tissue edema was still present (asterisk). The BCDVA was 20/200. At the 8-month follow-up (two months after silicone oil removal), the OCT imaging revealed that the retinal graft had been integrated with the surrounding retinal tissue (C), and the boundary between them was not clearly distinguishable. The BCDVA was 20/200. D: The B-scan OCT image taken at the last follow-up (18 months post-operative) showed complete anatomical closure of the MH with no evidence of EZ defect (preoperative EZ defect: 1485 µm) and a fully reconstructed external limiting membrane showing a characteristic step at the junction (white arrows). The BCDVA was maintained at 20/200.

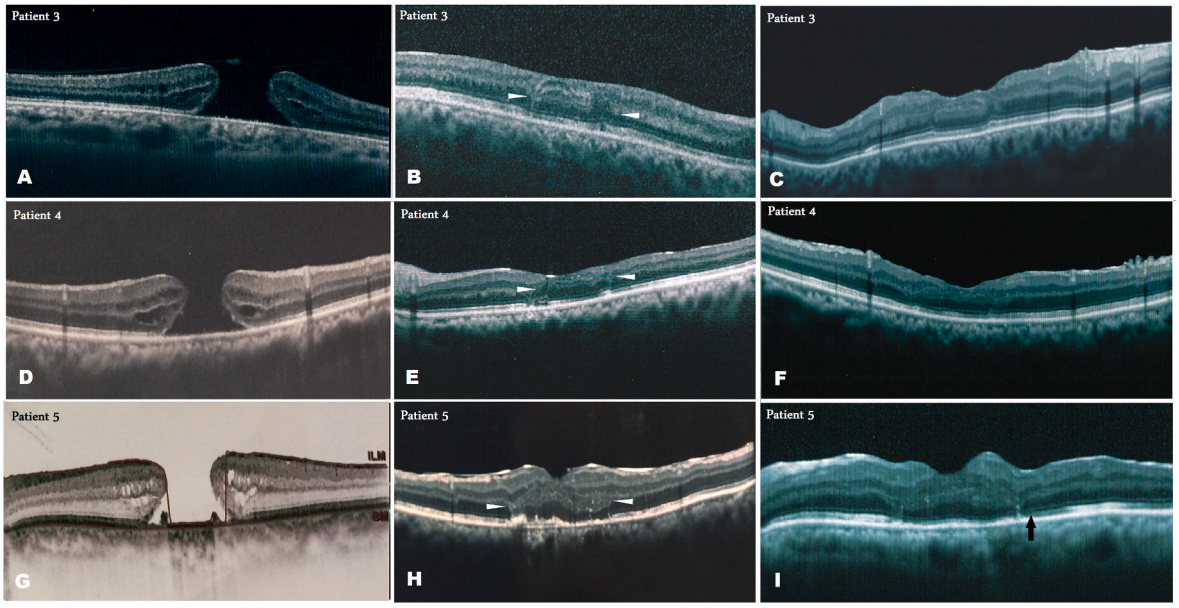

Fig. 3. Serial OCT findings and anatomical outcomes of ART surgery for patients 3 to 5. The preoperative optical coherence tomography (OCT) scans (A, D, G), showed macular holes (MHs) with basal diameters of 1339 μm, 1321 μm, and 1543 μm in patients 3, 4, and 5, respectively with a best corrected distant visual acuity (BCDVA) of 20/500 in all three patients. The postoperative OCT images (B, E, H) of these patients obtained with silicone oil in place demonstrated complete closure of the MHs and proper alignment of the internal retinal neural layers at the donor-recipient interfaces (arrow heads). Additionally, a new foveal pit formed at the donor area. C, F and I images taken at the last follow-up after silicone oil removal (12 months post-transplant surgery) demonstrated complete anatomical closure of the MH in all patients. There was no EZ defect in patients 3 and 4, and an EZ defect of only 100 μm in patient 5 (black arrow), with near completely reconstructed external limiting membrane in all patients. Moreover, there was improvement in BCDVA for all patients, which was maintained at a better value compared to their baseline values (20/150, 20/200, and 20/100).

migrating Müller cells secret neurotrophic and growth factors, which can increase the survival of the retinal neurons and photoreceptor cells.[24] Tabandeh's hypothesis for functional improvement of visual acuity included "flattening of the MH rim, partial centripetal migration of MH edges during the early healing phase, and further centripetal migration in the later phase associated with the shrinkage of the retinal graft and possibly by neuronal integration".[15] Grewal and Mahmoud, who defined ART in 2016, hypothesized that the retinal free flap acts not only as a scaffold for MH rim migration but also as a barrier that insulates the vitreous cavity from the subretinal space. In 2019, they showed the incorporation of the retinal graft, some migration of the surrounding retina, and partial restoration of EZ and ELM by OCT.[12,14] Reviewing the results of published studies, Patel et al. proposed that the reduction of central scotoma documented by microperimetry and conversion to a negative Watzke-Allen test by this surgical technique may act through cellular regeneration and ectopic synaptogenesis,[45] differentiation of retinal progenitor cell, integration and transfer of retinal progenitor cells to host neurons and finally closure of the MH with active neural tissue.[46] However, improvement in visual acuity is probably limited by the PR density/sensitivity of the midperipheral transplanted retina, or the shrinkage of the surrounding retina, whichever could attain a better vision.

Our study was limited by several factors, such as the small number of patients, retrospective nature of the study, absence of a comparison group, and the lack of standardized ancillary tests such as microperimetry and multifocal electroretinography. Furthermore, one patient had a short follow-up period, although other patients were followed for more than one year. Additionally, it should be noted that some of the patients in our study underwent crystalline lens removal simultaneously with MH surgery. This concurrent procedure might have played a role in contributing to the observed visual improvement to some extent.

5. Conclusions

The ART procedure accompanied by BCZ injection can be an effective method in the management of primary extra-large chronic FTMHs. Our modified technique allows for restoration of macular anatomy and continuity of ELM and EZ lines, with promising results in anatomical closure of MH. Future comparative studies are warranted to determine a size threshold, above which the ART might be the technique of choice.

Claim of priority

We conducted a thorough literature review on December 2023 utilizing PubMed, Medline, Google Scholar, and other search engines using all relevant key words pertaining to macular hole surgery and autologous retinal transplantation, yet we did not find any prior reports of such a method in the literature.

CRediT authorship contribution statement

Hossein Ashraf: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Sezaneh Haghpanah:** Writing – review & editing, Writing – original draft, Validation, Investigation, Formal analysis, Data curation. **Mohammad Hossein Nowroozzadeh:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation.

Patient consent

Written informed consent was obtained from all individual participants included in the study. All patients signed informed consent regarding publishing their data and photographs in the journals.

Ethics approval

This study was conducted in accordance with the Helsinki Declaration and was approved by the Ethics Committee of Shiraz University of

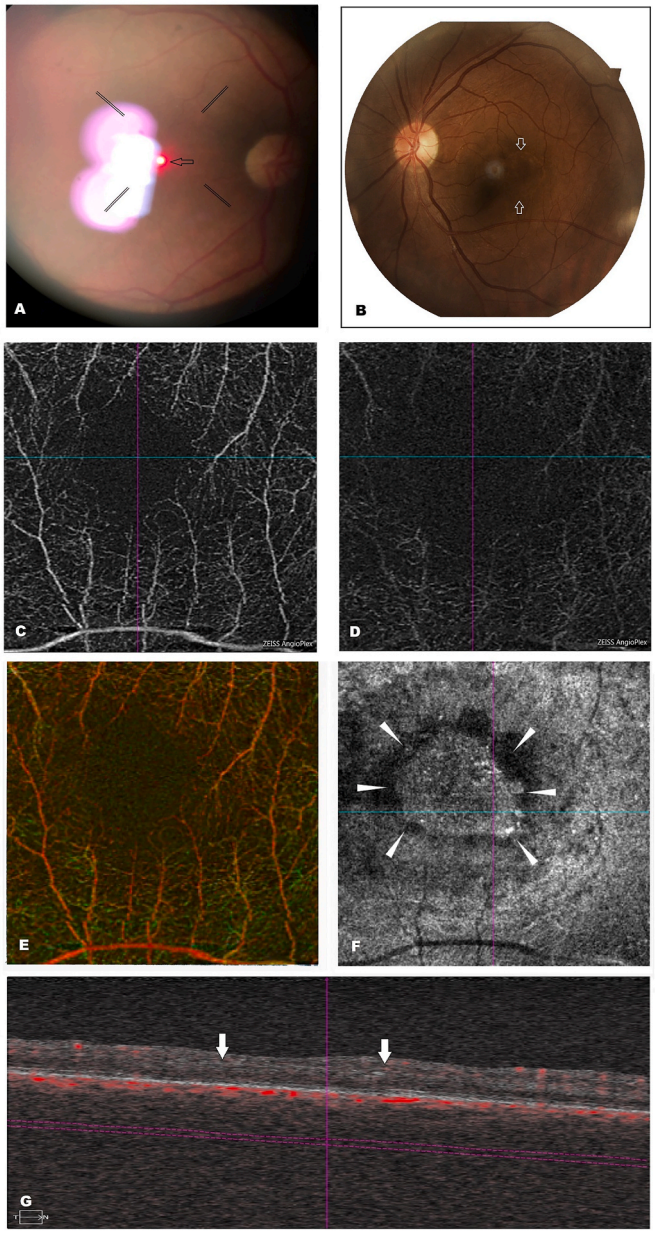

Fig. 4. Integration and functioning autologous retinal graft. A: Photographic demonstration of laser beam test over the grafted retinal tissue. The 100 μm laser beam (black empty arrow) could be perceived by 60 % of maximum beam intensity of laser system in patient 3. B: Color fundus photography of the transplanted retinal patch which has been merged to the surrounding macular tissues (white empty arrows) in patient 4. C to G: Optical coherence tomography angiography (Zeiss Cirrus HD-OCT 5000, Oberkochen, Baden-Württemberg, Germany) and en-face structural image OCT-A demonstrating normal picture of the superficial foveal vasculature (C) and surviving grafted retinal tissue (arrowheads) with early peripheral vascular perfusion of the transplanted retinal patch from the deep retinal vascular plexus (D–F). G: OCT-angiography B-scan revealed low-flow vascular perfusion signals at the periphery of the retinal graft (Patient 3) (white arrows). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

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Data availability statement

All data generated or analyzed during this study are included in this article and are available from the corresponding author on reasonable request.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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