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RETINAL DISORDERS

Lamellar macular holes: surgical outcome of 106 patients with long-term follow-up

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Abstract

Purpose To determine long-term results of vitrectomy for lamellar macular holes (LMH). To evaluate how the type of lamellar macular hole (tractional vs. degenerative) and the crystalline lens status might influence visual outcomes.

Methods We collected data from 106 patients with symptomatic lamellar macular hole that underwent pars plana vitrectomy with membranectomy and internal limiting membrane peeling. Best-corrected visual acuity (BCVA) and optical coherence tomography appearance were determined preoperatively and postoperatively.

Results Most of the lamellar holes were of tractional type (65%). Mean follow-up after surgery was 36 months. Mean BCVA increased from 20/50 to 20/43 at 6 months and 20/33 at last follow-up visit ($p < 0.001$). Vision improved in 74 (70%), remained stable in 11 (10%), and decreased in 21 (20%) eyes. Subgroup analysis showed that visual acuity significantly increased in the tractional but not in the degenerative forms of LMH. Thirteen eyes lost two or more ETDRS lines after surgery. Preoperative phakic/pseudophakic status influenced the functional outcomes.

Conclusions Surgery may be effective in some subsets of patients with lamellar macular hole, but postoperative visual loss is not uncommon and prospective controlled studies are warranted.

Keywords Epiretinal membrane · Internal limiting membrane · Lamellar macular hole · Lamellar hole-associated epiretinal proliferation · Pars plana vitrectomy

Introduction

Lamellar macular holes are a clinical entity first described by Gass in 1975 [1]. Optical coherence tomography (OCT) shed light on the morphological details of lamellar holes in more recent times [2]. Although their description varies among authors, lamellar macular hole may be defined as a partial-thickness defect of the macula caused by separation between outer and inner retinal layers [3]. An epiretinal membrane is usually associated with this condition, and a peculiar "lamellar hole-associated epiretinal proliferation" (LHEP) may be found [4, 5]. Consensus among scientists over the pathogenesis of lamellar macular holes has not been reached. A classification of two subtypes of lamellar defects has been recently proposed: "tractional" vs. "degenerative" [6]. The tractional form is characterized by "macular schisis-like" appearance, tractional epiretinal membrane, and intact ellipsoid layer. Degenerative type often presents intraretinal cavitation, non-tractional epiretinal proliferation, and ellipsoidal line disruption (Fig. 1).

Most patients with a lamellar macular hole experience mild central visual loss and/or metamorphopsia, and the lesion remains stable on OCT over the years. A small portion of patients with lamellar macular defects may develop more severe visual impairment and/or show anatomical signs of progression on OCT. Few of these cases may progress into a full thickness macular hole [2]. Surgical treatment of LMHs is controversial [7–18]. We herein present a retrospective analysis of 106 symptomatic lamellar macular holes that underwent surgical treatment.

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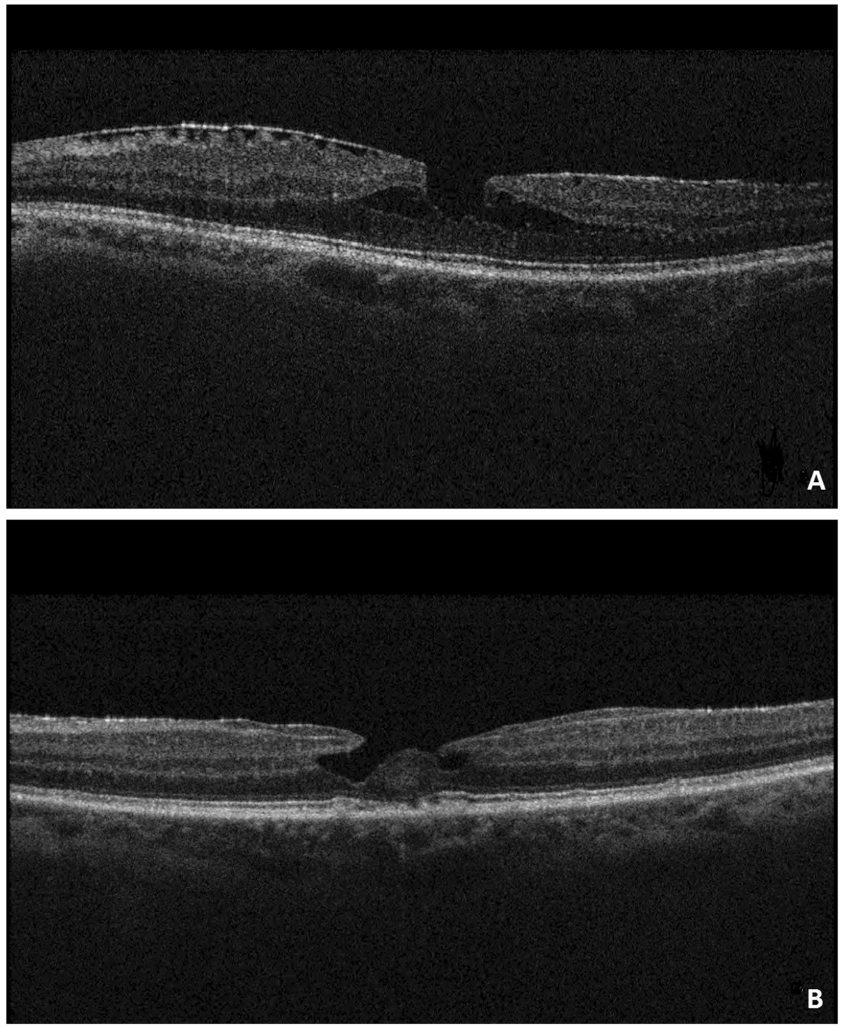

Fig. 1 Optical coherence tomography features of tractional and degenerative lamellar macular hole. Tractional lamellar macular hole characterized by epiretinal membrane with surface wrinkling, sharp intraretinal split, and "schisis-like appearance" (**a**). Degenerative lamellar macular hole identified by round-edged intraretinal cavitation, "foveal bump," and epiretinal proliferation of medium reflectivity (**b**)

Methods

After the approval of the Provincial Ethical Committee of Reggio Emilia, we searched our electronic register of patients that underwent retina surgery for the words: "lamellar" and "macular hole". Among 3947 eyes operated between January 2006 and December 2015, 348 eyes were found, and the corresponding clinical charts and OCT images were reviewed.

Patients with a preoperative OCT demonstrating a lamellar macular hole were included. Morphological OCT criteria for diagnosis of LMH were (1) irregular foveal profile; (2) splitting between retinal layers; and (3) absence of a full-thickness foveal defect. OCT images were obtained using the Stratus OCT (Carl Zeiss Meditec, USA) and, starting in 2012, the 3D OCT-2000 (Topcon, Japan). In order to be included in this study, the following were also required: (1) preoperative OCT image demonstrating a LMH; (2) preoperative best-corrected visual acuity (BCVA); (3) postoperative follow-up of minimum 1 month; (4) postoperative BCVA. Patients were excluded if one of these four criteria was not meet.

The following preoperative conditions were reasons for exclusion: previous retinal episcleral or vitreous surgery, diabetic retinopathy, full-thickness macular hole, vitreomacular traction syndrome, retinal detachment, age-related macular degeneration other than mild or moderate forms, choroidal neovascularization, high myopia (> 6D), myopic foveoschisis, or corneal opacity. Cases of epiretinal membranes with a pseudohole configuration on OCT were carefully excluded.

OCT images were sent to the University of California, San Francisco, USA, and were independently reviewed by two senior ophthalmologists (MC, JMS). Cases were excluded if reviewers were not in agreement. Lamellar macular holes were classified as tractional, degenerative, or mixed, according to Govetto et al. [6]. Diagnosis of tractional or degenerative LMH was made if a minimum of 3 out of 5 OCT criteria were found, as described by Govetto using a spectral-domain OCT. When only the Stratus (time-domain) OCT images were available, the ellipsoid defect criterion was excluded, and diagnosis was conservatively made with a minimum of 3 out of 4 criteria. The LMH was classified as "mixed" if it did not match these criteria [6].

The following data were collected from clinical charts and OCT images: patient's age and gender; operated eye; time of surgery; time of last follow-up visit; preoperative BCVA and central macular thickness (CMT); last available postoperative BCVA and/or CMT; ocular axial length; presence of LHEP; ellipsoidal layer disruption (only if spectral-domain OCT images were available); lamellar macular hole resolution with recognizable foveal contour at last postoperative OCT scan; preoperative and postoperative phakic/pseudophakic status; variants in vitreous surgery technique (associated cataract surgery, staining of internal limiting membrane [ILM], tamponades); and postoperative complications.

Preoperatively, all patients were symptomatic and complained of worsening visual acuity and distortion. When possible, the decision to perform surgery was postponed, and follow-up visits were scheduled to confirm the decrease of visual acuity and/or changes on OCT. If cataract was suspected to be the main cause of the visual loss, phacoemulsification was recommended before considering vitreous surgery. Surgical approach was agreed upon after a discussion of treatment options between the surgeon and the patient. All patients included in this study underwent pars plana vitrectomy with ERM and ILM peeling under local anesthesia by one of five surgeons. Three surgeons performed standard cataract surgery with intraocular lens (IOL) implantation at the time of vitrectomy in all patients older than 60 years. In some cases, the following dyes were used to stain intraocular tissues: triamcinolone acetonide 4%, indocyanine green dye 0.05%, trypan blue 0.15%, trypan blue 0.15% plus brilliant blue G 0.025%. At the end of surgery, air–fluid exchange was performed at the surgeon's discretion and eventually followed by air–gas exchange. An isoexpansile mixture of sulfur hexafluoride gas (SF_6) or perfluoropropane gas (C_3F_8) was used. Postoperatively, these patients were requested to remain face down for 3 to 7 days.

Statistical analysis was conducted using STATA software (v.12.0, STATA Corp., USA). Snellen visual acuity was converted to the logarithm of the minimum angle of resolution (LogMAR). Two-tailed paired Student's t test was performed to compare continuous variables. Chi-square test was used to compare categorical variables. Results were expressed as mean ± standard deviation. A p value < 0.05 was considered statistically significant.

Results

General results One-hundred and six eyes with a symptomatic lamellar macular hole operated in our institution met the above-mentioned inclusion/exclusion criteria. Seventy-four patients were female (69%); 58% were right eyes. Four patients had surgery in both eyes. Median age of patients was 71 (mean 71.4, range 55–87) years. Sixty-nine of the lamellar holes were of tractional type (65%), 19 were of degenerative type (18%), and 18 were of mixed type (17%). Lamellar hole-associated epiretinal proliferation was present in 58% of degenerative type LMHs.

Mean follow-up after surgery was 36 (median 25, range 1–116) months; 89% of the eyes were followed for at least 6 months.

Visual acuity at last follow-up Preoperative mean BCVA was 0.45 ± 0.24 LogMAR (Snellen fraction 20/50; range 20/400 to 20/25). Postoperative mean BCVA increased to 0.31 ± 0.34 LogMAR (Snellen fraction 20/33; range 20/400 to 20/20) and the difference was statistically significant when compared to preoperative values (p = 0.00001; Fig. 2). After surgery, vision improved in 74 eyes (70%), remained stable in 11 (10%), and decreased in 21 (20%) eyes. BCVA increased postoperatively by at least 0.2 LogMAR (corresponding to 2 or more ETDRS lines) in 56 eyes (53%). In 37 eyes (35%), BCVA improved after surgery by at least 0.3 LogMAR (3 or more ETDRS lines).

When considering LMH types, visual acuity improved after surgery in tractional (0.41 ± 0.19 vs. 0.25 ± 0.27 LogMAR; 20/51 vs. 20/36; n = 69; p < 0.00001) and mixed forms (0.46 ± 0.28 vs. 0.30 ± 0.35 LogMAR; 20/58 vs. 20/40; n = 18; p = 0.021) but not in degenerative type (0.61 ± 0.31 vs. 0.54 ± 0.44 LogMAR; 20/81 vs. 20/70; n = 19; p = 0.27) (Fig. 3). Visual acuity gain was directly correlated with preoperative visual acuity (p = 0.00045). Age, different retinal dyes, and tamponades did not significantly influence these results.

Visual acuity at 6 months follow-up Visual acuity was measured 6 months after surgery in 74 patients (72%); 20 patients had a follow-up longer than 6 months but skipped the 6-month follow-up visit; 12 patients had a follow-up shorter than 6 months. Postoperative mean BCVA at the 6 months follow-up visit significantly increased to 0.34 ± 0.27 LogMAR when compared to baseline (p = 0.0002).

When considering LMH types at the 6-month follow-up visit, visual acuity improved after surgery in tractional (0.41 ± 0.19 vs. 0.30 ± 0.25 LogMAR; n = 47; p = 0.0017) but not in degenerative (0.61 ± 0.31 vs. 0.48 ± 0.34 LogMAR; n = 14; p = 0.07) and mixed forms (0.46 ± 0.28 vs. 0.33 ± 0.22 LogMAR; n = 13; p = 0.08).

Phakic/pseudophakic status At the last follow-up visit, 87 eyes were pseudophakic (Fig. 4): 18 eyes were already pseudophakic at the time of vitreous surgery for LMH (17%; group A); 39 eyes had cataract surgery with IOL implantation combined with vitrectomy for LMH (37%; group B); 30 eyes had cataract surgery several months after vitrectomy, during the follow-up period of this study (28%; group C). Nineteen eyes were still phakic at last follow-up visit (18%; group D).

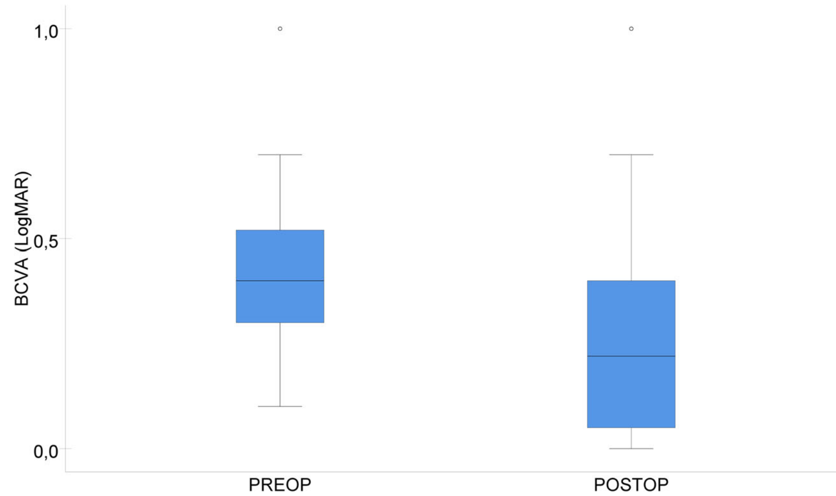

Fig. 2 Best-corrected visual acuity before surgery for lamellar macular hole and at the last follow-up visit. Preoperative mean BCVA was 0.45 ± 0.24 LogMAR (Snellen fraction 20/50; range 20/400 to 20/25). At last follow-up visit, postoperative mean BCVA increased to 0.31 ± 0.34 LogMAR (Snellen fraction 20/33; range 20/400 to 20/20). The difference was statistically significant ($p = 0.00001$)

When only eyes in groups A, C, and D were included (in order to exclude combined phaco-vitrectomy cases [group B] from analysis), the difference between preoperative and postoperative mean BCVA was statistically significant (0.44 ± 0.24 vs. 0.33 ± 0.35 LogMAR; 20/55 vs. 20/43; $n = 67$; $p = 0.0036$).

Eyes in group B demonstrated a significant improvement in BCVA at last follow-up visit (0.46 ± 0.25 vs. 0.24 ± 0.30 LogMAR; 20/58 vs. 20/35; $n = 39$; $p = 0.00016$) as well as the eyes in group C (0.54 ± 0.28 vs. 0.32 ± 0.34 LogMAR; 20/69 vs. 20/42; $n = 30$; $p = 0.000017$). Surgery for LMH had no significant impact on visual acuity in eyes of group A (0.34 ± 0.14 vs. 0.39 ± 0.44 LogMAR; 20/44 vs. 20/49; $n = 18$; $p = 0.30$) and group D (0.38 ± 0.17 vs. 0.31 ± 0.25 LogMAR; 20/48 vs. 20/41; $n = 19$; $p = 0.16$). When only eyes with the tractional form of LMH were considered in group A, an increase of mean BCVA after surgery could be demonstrated (0.35 ± 0.16 vs. 0.25 ± 0.26 LogMAR; 20/45 vs. 20/36; $n = 12$; $p = 0.04905$).

Causes of visual loss A list of all patients that experienced visual loss after surgery is presented in Table 1. Among the 21 eyes where vision decreased postoperatively, 8 lost one ETDRS line, 2 lost two lines, and 11 lost three or more ETDRS lines.

Postoperatively, three patients developed a full-thickness macular hole and one patient a retinal detachment. One patient underwent cataract surgery during vitrectomy, experienced posterior capsule rupture, and developed postoperative cystoid macular edema. Two other patients demonstrated persistence of mild cystoid macular edema. Six patients with low vision after surgery had significant cataract or posterior capsule opacification at last follow-up visit. One woman had surgery bilaterally with visual improvement and, after years, developed age-related macular degeneration in both eyes.

OCT evaluation Postoperative cross-sectional OCT images were available for 84 eyes and showed a reconstituted foveal pit with no retinal splitting in 55 eyes (66%). Mild ellipsoidal layer disruption was seen on spectral-domain OCT in 4 cases after surgery. Mean central macular thickness was significantly reduced postoperatively when paired *t* test was calculated separately for time-domain and spectral-domain data sets: 316 ± 89 vs. 282 ± 73 μm ($n = 33$; $p = 0.025$) and 342 ± 72 vs. 300 ± 55 μm ($n = 38$; $p = 0.00002$), respectively (Fig. 5).

Other results Most of the vitrectomies were performed using a 23-gauge system (82%). During surgery, intravitreal triamcinolone was utilized in 26 eyes. Trypan blue combined with brilliant blue dye was used in 49 eyes (46%), trypan blue in 27 eyes (26%), and indocyanine green dye in 24 eyes (23%). As tamponade, SF_6 was employed in 74 eyes (70%) and C_3F_8 in 11 eyes (10%). No significant differences were demonstrated among these groups, except for the eyes where indocyanine green dye (ICG) was used. In eyes where the ILM was stained with ICG, postoperative visual acuity improved at the 6-month follow-up but not at the final visit when compared to the preoperative BCVA (0.46 ± 0.23 vs. 0.31 ± 0.27 LogMAR, $p = 0.0032$; and 0.46 ± 0.23 vs. 0.39 ± 0.38 LogMAR, $p = 0.17$, respectively; $n = 24$). Vision increased after surgery both at 6-month and at the last follow-up visit in eyes where other dyes rather than ICG were used (0.45 ± 0.25 vs. 0.34 ± 0.27 LogMAR, $p = 0.0016$; and 0.45 ± 0.25 vs. 0.28 ± 0.32 LogMAR, $p = 0.0000072$, respectively; $n = 82$).

Discussion

It is debated whether lamellar macular holes are a stable condition and whether they should be surgically treated. Most of the studies on their natural history concluded that LMHs are a

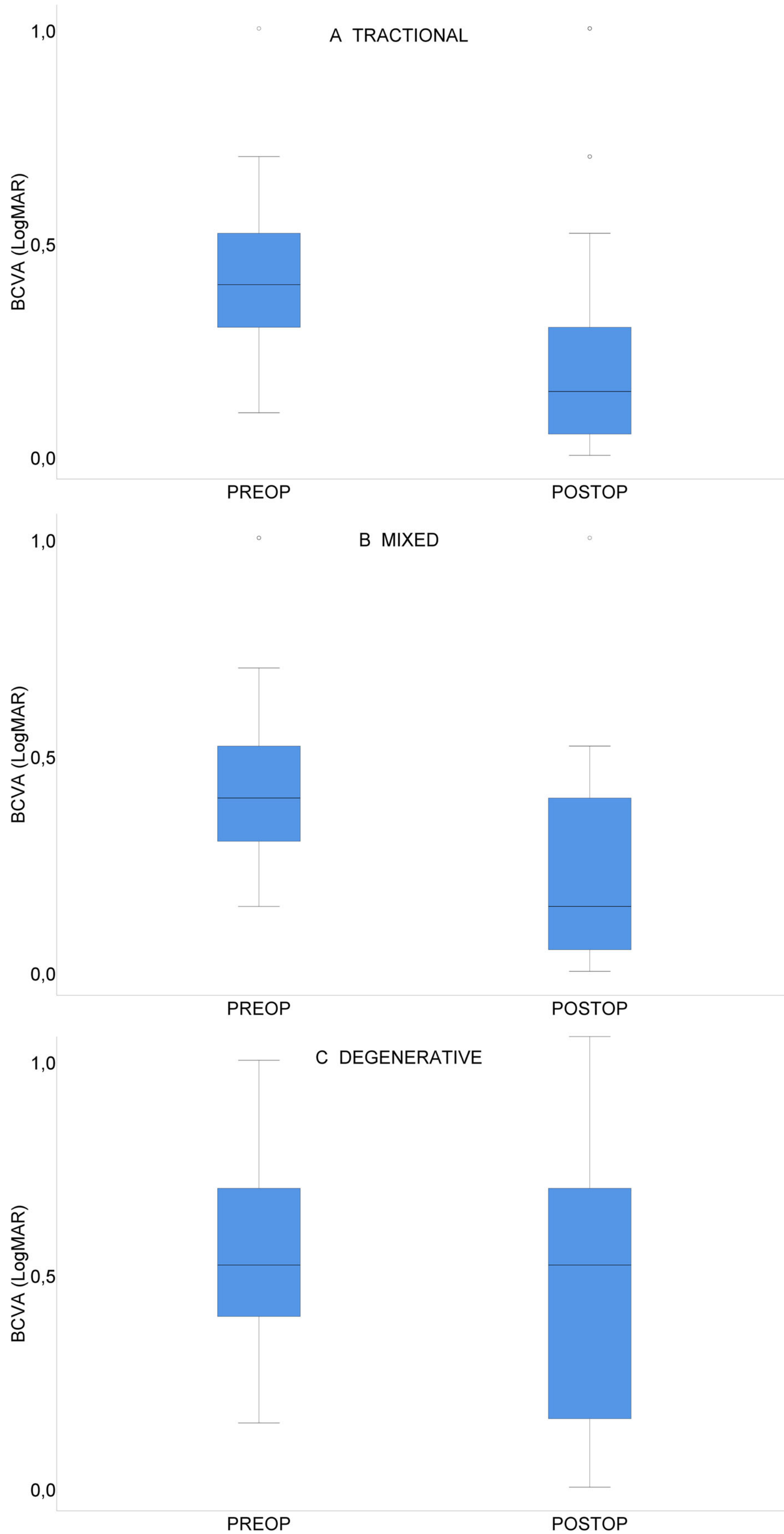

Fig. 3 Postoperative visual outcomes according to lamellar macular hole type. Vision at the last follow-up visit was affected by the type of LMH. Mean best-corrected visual acuity improved after surgery in tractional (0.41 ± 0.19 vs. 0.25 ± 0.27 LogMAR; 20/51 vs. 20/36; $n = 69$; $p < 0.00001$; (**a**)) and mixed forms (0.46 ± 0.28 vs. 0.30 ± 0.35 LogMAR; 20/58 vs. 20/40; $n = 18$; $p = 0.021$; (**b**)) of lamellar macular hole but it did not in the degenerative type (0.61 ± 0.31 vs. 0.54 ± 0.44 LogMAR; 20/81 vs. 20/70; $n = 19$; $p = 0.27$; (**c**))

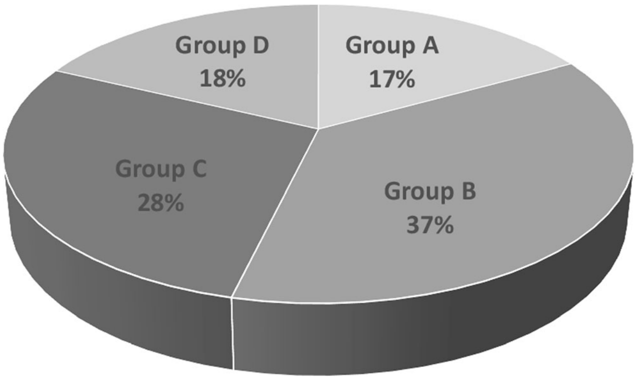

Fig. 4 Status of the crystalline lens at the last follow-up visit. Eighty-seven eyes were pseudophakic at the final clinical examination (82%). Among them, 18 eyes were already pseudophakic at the time of vitreous surgery for LMH (17%; group A); 39 eyes had cataract surgery with IOL implantation at the time of vitrectomy (combined phaco-vitrectomy; 37%; group B); 30 eyes had cataract surgery several months after surgery for LMH (30%; group C). Nineteen eyes were still phakic at last follow-up visit (18%; group D)

slowly progressing clinical entities [2, 4, 6, 19–22]. A review of the surgical reports including more than 15 LMHs showed generally positive outcomes [7–10, 12–14, 18, 20, 23–25] but with notable exceptions and caveats [15–17] and severe limitations (small number of patients, unreported lens status, unclear inclusion criteria).

In our analysis of 106 lamellar macular holes treated by vitrectomy, mean BCVA increased from 20/50 to 20/43 at 6 months ($p = 0.0002$) and 20/33 at last follow-up visit ($p = 0.00001$). Subset analysis showed that visual acuity significantly increased in the tractional but not in the degenerative forms of LMH.

Efforts were made in order to find out whether the lens status could have had a role in these results. Most of the patients (82%) were pseudophakic at the last follow-up visit, suggesting that our data were not significantly influenced by cataract. Thirty-nine eyes underwent cataract surgery at the same time with vitrectomy and showed good outcomes (from 20/58 to 20/35; $p = 0.00016$; group B). Although we did not recommend vitrectomy if cataract was believed to be the primary cause of visual loss in patients with LMH, it is possible that vision improved in these subjects because of the removal of the senile crystalline lens. When these eyes were excluded

Table 1 Characteristics of patients that experienced visual loss after surgery for lamellar macular hole

Pt ID	Age (years)	Sex	Eye	LMH type	LHEP	CMT pre (microns)	CMT post (microns)	Follow-up (months)	BCVA pre (LogMAR)	BCVA post (LogMAR)	Cataract surgery	Complication
1	70	F	R	T	–	–	259	83	0.52	0.70	Post	Foveal splitting persists
2	56	M	R	D	–	214	260	46	0.15	0.22	Post	None
3	69	F	R	T	–	353	266	3	0.52	1.00	No	Cataract
4	69	M	L	D	Yes	253	–	75	1.00	1.30	Post	Full-thickness macular hole
5	62	F	L	T	–	317	234	90	0.70	1.00	Post	Posterior capsular opacity
6	70	F	L	D	Yes	234	330	17	0.52	1.00	No	Full-thickness macular hole
7	75	F	R	M	–	163	198	52	0.52	1.30	Pre	Dry AMD
8	82	F	L	T	–	246	528	67	0.40	1.00	Pre	Wet AMD
9	83	F	R	T	–	276	215	60	0.15	0.40	Same	Dry AMD
10	59	M	L	M	–	221	–	6	0.40	0.52	No	Cataract
11	75	F	R	T	–	311	–	1	0.40	0.52	Same	Short follow-up
12	59	F	L	D	–	318	–	1	0.40	0.70	No	Short follow-up
13	80	F	L	T	–	250	–	2	0.15	0.22	No	Cataract
14	61	F	R	T	–	279*	–	9	0.05	0.22	No	Cataract
15	67	F	R	D	–	235*	246*	36	0.30	1.30	Pre	Retinal detachment
16	76	F	R	T	–	456*	430*	10	0.30	1.00	Same	Cystoid macular edema
17	77	M	R	T	–	366*	308*	10	0.15	0.30	Same	Scotoma[a]
18	74	F	L	D	Yes	227*	206*	7	0.52	1.30	Same	Full-thickness macular hole
19	61	F	R	T	–	360*	307*	9	0.22	0.30	No	Cataract
20	81	F	R	T	–	332*	366*	3	0.15	0.22	Pre	Cystoid macular edema
21	79	M	R	T	–	411*	268*	11	0.70	1.00	Pre	Dry AMD

Vision decreased postoperatively in 21 eyes: 8 lost one ETDRS line, 2 lost two lines, and 11 lost three or more ETDRS lines

Pt ID patient number, *R* right eye, *L* left eye, *LMH type* lamellar macular hole, *T* tractional, *D* degenerative, *M* mixed, *LHEP* lamellar hole-associate epiretinal proliferation, *CMT pre/post* central macular thickness measured by TD-OCT before surgery and at last follow-up visit, *BCVA pre/post* best-corrected visual acuity before surgery and at last follow-up visit, *Cataract surgery: Pre* done before vitrectomy for LMH, *Same* done at the same time, *Post* done months after vitrectomy, *No* phakic

[a] Papillomacular bundle defect

*SD-OCT values

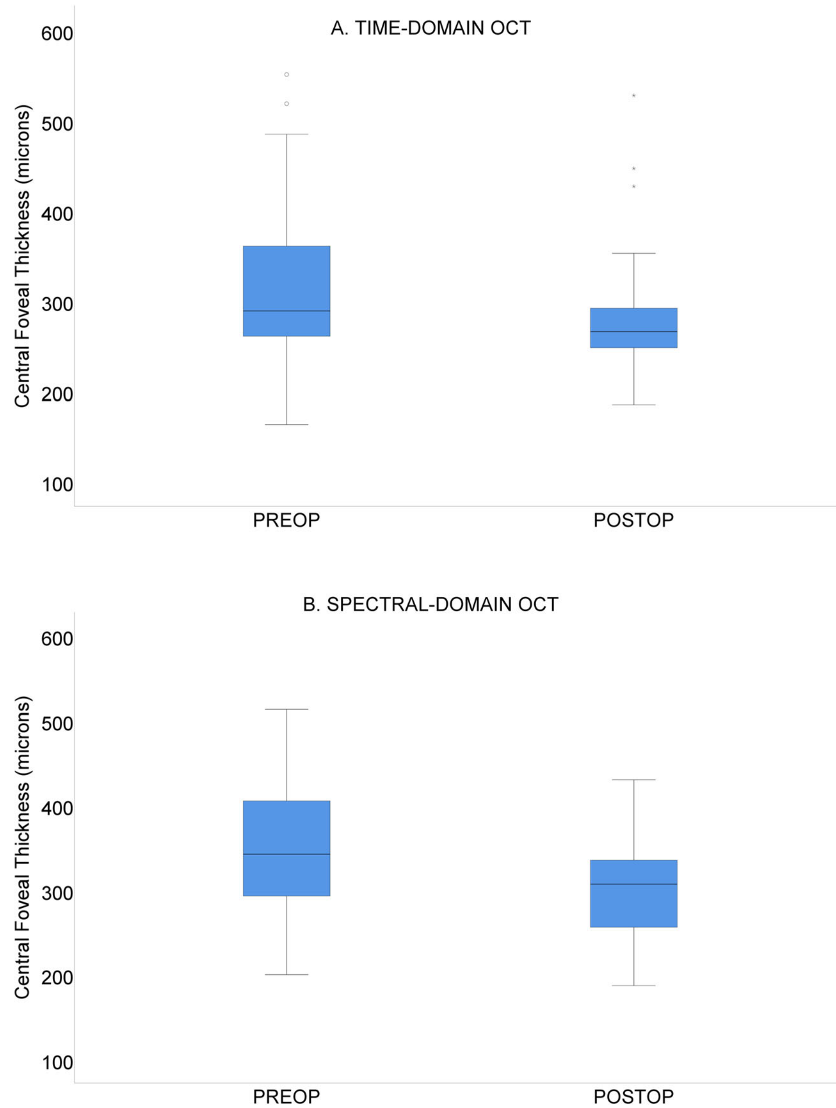

Fig. 5 Effects of vitreous surgery for lamellar macular holes on macular thickness measured by optical coherence tomography. Mean central foveal thickness was significantly reduced at last follow-up visit when compared to preoperative values. Paired *t* test was calculated separately for patients that were followed by time-domain OCT (316 ± 89 vs. 282 ± 73 μm; $n = 33$; $p = 0.025$; (**a**)) and spectral-domain OCT (342 ± 72 vs. 300 ± 55 μm; $n = 38$; $p = 0.00002$; (**b**))

from analysis, the postoperative improvement in mean BCVA was still significant ($n = 67$; $p = 0.0036$; groups A, C, and D).

Thirty eyes with no cataract at the time of vitrectomy for LMH eventually developed cataract in the postoperative period and underwent standard phacoemulsification with IOL implantation (group C). Visual acuity significantly improved at last follow-up visit in these patients ($p = 0.000017$).

Nineteen eyes were still phakic at the last visit (group D). Vision did not significantly improve postoperatively in this group (from 20/48 to 20/41; $p = 0.16$), likely because of the cataractous changes induced by vitrectomy.

Eyes that were already pseudophakic at the time they underwent vitrectomy for LMH did not show an improved visual acuity at last follow-up visit ($p = 0.30$). The use of ICG for ILM staining had no apparent effect on this subgroup ($n = 6$). We believe that this result is due to peculiar characteristics of these eyes. These patients were significantly older than the others ($p = 0.041$). All these eyes demonstrated an improvement of visual acuity at last follow-up visit, except for three that developed age-related macular degeneration and one that developed a retinal detachment. Reviewing the charts of the patients that developed AMD, we realized that BCVA always improved within 6 months from surgery, but decreased years later because of AMD (median follow-up 52 months). When only eyes with the tractional form of LMH were considered in this group, a moderate increase of mean BCVA after surgery could be demonstrated (20/45 to 20/36; $p = 0.04905$), in line with our general conclusions.

Twenty-one eyes (20%) experienced a form of visual loss after surgery for LMH, with 11 eyes losing three or more ETDRS lines (Table 1). In particular, three patients developed a full-thickness macular hole and one patient a retinal detachment. Low vision at last follow-up visit was due to a treatable cause such as cataract in six patients. Two eyes had a very short follow-up and could possibly have improved thereafter. Three eyes developed severe age-related macular degeneration many years after surgery. ICG staining for ILM was used in 8 out of these 21 eyes, possibly confirming what already described by Haritoglou et al. [26].

Limitations of this study include its retrospective nature; multiple surgeons with slightly different surgical techniques; no data on the vitreous status (presence of preoperative posterior vitreous detachment); and no information on the fellow eye. Cataract removal at the time of vitreoretinal surgery may also represent a confounding factor and/or increase the post-operative inflammation. Nevertheless, combined surgery is routinely performed in non-US nations and this may better represent "real-life" situations giving practical guidance to the surgeons. On the other side, the very high proportion of pseudophakic eyes at the final follow-up visit provides a clear and stable picture of the surgical outcomes. Measurements of morphological details of LMHs at OCT that can be found in other publications [11, 13, 22], were not performed in this study.

We conservatively conclude that a select group of patients with symptomatic lamellar macular hole and significant epiretinal traction may benefit from surgery. Vision in lamellar macular holes of degenerative type seems not to improve after surgery. Although this conclusion may be biased by the small number of included cases ($n = 19$), our results are in line with other publications [20, 24, 25]. We underline that one fifth of patients operated for lamellar macular hole may experience visual loss. After surgery, the occurrence of a full-thickness macular lesion is not uncommon. Although our data provide insights into the role of surgical intervention for lamellar macular holes, prospective controlled studies are warranted to establish the correct management of these patients.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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