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Long-term functional and anatomical outcomes following macular hole surgery: 5-year follow-up study

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Long-term functional and anatomical outcomes following macular hole surgery: 5-year follow-up study

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Abstract

Introduction: To characterize anatomical and functional long-term outcomes following macular hole (MH) surgery.

Methods: Retrospective chart review of forty-four eyes of 44 patients diagnosed with macular hole (MH) who underwent MH surgery at a tertiary referral center. Standard pars plana vitrectomy with simple internal limiting membrane (ILM) peeling, gas tamponade and face-down positioning was performed. Cataract surgery was done simultaneously with macular hole surgery or during follow-up if a visually significant cataract developed. Exclusion criteria included previous vitrectomy, traumatic MHs, retinal detachment or MHs associated with high myopia. Baseline and follow-up examinations at 6 months and 5 years included evaluation of best-corrected visual acuity (BCVA) in ETDRS letters and serial OCT imaging, assessed by two independent graders.

Results: We included 44 eyes from 44 patients (59.1% female, age 66.9±9.8 years) in the study. Mean sample BCVA letter score was 36.2±13.4 letters at baseline. Mean MH size (minimum linear diameter) was 515,0±194,2 μm and 4.5% were small MHs (<250 μm), 27.3% were medium MHs (250-400 μm) and 68.2% were large MHs (> 400 μm). MH closure at the end of follow-up was 90.9% (40/44 eyes). Non-closure cases (4/44) were all large macular holes. Mean individual BCVA improvement, compared to baseline, was +21.2±16.1 letters at 6 months (p<0.001) and +25.4±18.5 letters at 5 years (p<0.001). Compared to the 6 months timepoint, visual acuity significantly improved at 5 years (+5.0±12.1 letters, p=0.024). Overall, 86.4% (38/44) improved BCVA more than 5 letters, 9.1% (4/44) maintained BCVA within 5 letters and only 4.6% (2/44) lost more than 5 letters at the end of follow-up. At the end of the study, visual acuity improvement did not differ by lens status (pseudophakic

+24.3±16.4 letters vs phakic +27.9±23.4 letters, p=0.563). Central macular thickness (CMT) significantly decreased with follow-up, with a reduction of -37.1±83.9 µm at 6 months (p=0.037) and -50.0±80.3 µm at 5 years (p<0.001).

Conclusion: To the best of our knowledge, we present the largest long-term cohort on functional and structural outcomes following MH surgery. A high MH closure rate was achieved in this cohort. Visual acuity not only remained stable at 5 years of follow-up, but also seemingly improved from the early 6 months post-operative period.

Keywords

Macular hole, vitrectomy, optical coherence tomography, visual and anatomical outcomes

Introduction

A macular hole (MH) is a discontinuity of the neurosensory retina that develops in the center of the macula, leading to metamorphopsia and poor visual acuity. It is believed that macular holes are caused by pathologic vitreoretinal traction at the fovea.[1,2]

Macular holes can be idiopathic, traumatic or consequence of other ophthalmic diseases. Idiopathic holes are the most common, representing approximately 85% of cases.[3,4] While mostly presenting unilaterally, bilateral holes do occur in 10-20% of cases. Absolute prevalence ranges between 0,2 to 3,3 per 1,000 people[3,4], most frequently affecting women (2:1) in their seventieth decade of life.[4]

Optical coherence tomography (OCT) is a fundamental tool for diagnosis and management of macular holes, enabling better understanding of associated vitreoretinal interface disorders and aiding in monitoring and surgical decisions. Furthermore, it also enables accurate measurements of the macular hole itself that can, at least in some studies, predict anatomical and functional outcomes, namely base diameter, macular hole inner opening and minimum diameter, which seem to be associated with both anatomical and visual success.[5] Adequate classification of the macular hole and accompanying status of the vitreoretinal interface is also essential. Commonly, the classifications proposed by Gass[6] or The International Vitreomacular Traction Study (IVTS) Group[7] are used (Table 1). Uchino[8] classification is also used, but to define the state of the vitreoretinal interface and not properly the macular holes.

Gass' classification divides idiopathic macular holes into 4 stages based on clinical findings. Stage 1 macular hole, also known as impending macular hole, is considered precursor of full thickness macular hole, and it is divided into 2 substages, 1A and 1B. Stage 1A appears as a yellow spot in the center of the fovea and stage 1B appears as a yellow ring. Stage 2 is the full thickness hole of less than 400 μm in size. More than 400 μm in size with vitreomacular attachment (VMA) defines stage 3 which becomes a stage 4 macular hole once a complete posterior vitreous detachment occurs with detachment of the posterior vitreous hyaloid from the entire macula and optic disc.[9]

Comparing Gass's classification with the more recent IVTS's classification, stage 0 corresponds to a vitreomacular adhesion, stage 1 to vitreomacular traction (VMT), stage 2 to a small (minimum linear diameter with ≤250 μm) or medium (minimum linear diameter between >250 and ≤400 μm) hole with VMT, stage 3 to a medium or large (minimum linear diameter with >400 μm) hole with VMT and stage 4 to a macular hole without VMT.[7]

Uchino's classification uses the condition of the posterior vitreoretinal interface and divides it into 5 stages (0 to 4). Stage 0 is defined by the VMA. Stage 1 was defined by incomplete focal perifoveal posterior vitreous detachment (PVD). Stage 2 is defined by incomplete perifoveal PVD in all quadrants with persistent attachment to the optic nerve head. Stage 3 is a detachment of the posterior vitreous face from the fovea and stage 4 is a complete PVD.[10]

The natural untreated history of macular holes is associated with poor central visual acuity, while vitrectomy leads to good functional and anatomical results in 85% to 90% of cases.[3,11] Surgical treatment of idiopathic full thickness macular holes by vitrectomy was initially described in 1991 by Kelly and Wendel. Its basic technique, which includes posterior vitrectomy via pars plana, removal of the posterior hyaloid, internal limiting membrane (ILM) peeling, fluid-air, gas tamponade and post-operative ventral decubitus has been largely maintained to the present day.[12–14] Later the inverted ILM flap technique was added and apparently appears to improve the anatomical and functional results, especially in the larger holes.[15] Despite many studies having reported on the effectiveness of vitrectomy in macular holes, follow-up periods were limited to 6 or 12 months. To our knowledge, only Sakaguchi *et al*[16] have reported a 5 years follow-up period (83,4±10,5 months, ranging from 61 to 100 months) after surgery, however they did not examined OCT scans and consequently the macular and foveal microstructure after surgery. Albeit with smaller follow-up time (54±20 months, ranging from 21 to 91 months), Purtskhvanidze *et al*[13], besides assessing the best-corrected visual acuity (BCVA), they controlled central macular thickness (CMT) over that time, trying to correlate these two variables and other as we do. Accordingly, there is a gap in knowledge regarding long-term outcomes in macular hole surgery, being important to investigate whether macular surgery, which is proven to be associated with an immediate anatomical and functional improvement after surgery, does not have long-term side effects as yet poorly understood.

The aim of this study is to determine the long-term anatomic and visual outcomes in patients who underwent vitrectomy after 5 years of follow-up.

Table 1: Comparison of the different classifications for idiopathic macular holes (Adapted from H. Madi *et al*)

Gass stages	Gass classification	IVTS classification
0	VMA without any change in foveal architecture	VMA
1	Impending macular hole	VMT
2	≤400 µm with VMA	Small/Medium hole with VMT
3	>400 µm with VMA	Medium/Large hole with VMT
4	Complete PVD	Macular hole regardless the size without VMT

IVTS: International Vitreomacular Traction Study; PVD: posterior vitreous detachment; VMA-vitreomacular adhesion; VMT: vitreomacular traction

Methods

Retrospective chart review including patients who underwent vitrectomy for macular hole repair in a single eye at our institution between 2007 and 2012, all with 60 months (±6 months) of clinical and OCT follow-up. Exclusion criteria included previous vitrectomy, traumatic macular holes, retinal detachment or macular holes associated with high myopia (>6D spherical equivalent).

For each patient, BCVA was collected at baseline (before surgery), 6 months, 36 months (±6 months) and 60 months (±6 months) after surgery (end of follow-up for the present study). For the same timepoints, spectral domain optical coherence tomography (SD-OCT) was also analysed. SD-OCT images were obtained using Heidelberg Spectralis®. A minority of cases performed OCT imaging using the Zeiss Cirrus® HD-OCT 5000 SD-OCT device (and then appropriate thickness measurements were normalized to equivalent Spectralis measurements using conversion equations described by Giani *et al*[17]).

Visual acuity was measured using Snellen charts and afterwards converted to ETDRS letter scores (as described by Ninel *et al*[18]) for statistical analysis. Preoperatively, idiopathic macular holes were classified using Gass[6], Uchino[8] and IVTS Group[7] classifications. Furthermore, measurements of the macular hole inner opening diameter, minimum linear diameter, base diameter and macular hole height were made. The macular hole index (MHI) was derived from these data, using the equation MHI=hole height/base diameter (Figure 1)[5]. Central macular thickness (CMT) was also measured automatically by the OCT equipment. Finally, all scans were ascertained for the presence of cystoid macular edema (CME) and/or epiretinal membrane (ERM) and, in follow-up examinations, for anatomical closure of macular holes. All scans, before and after surgery, were retrospectively analyzed by two researchers (MG and MR) – the average of obtained measures was used for quantitative parameters. For qualitative evaluations, when agreement between observers was not attained, a third trained observer (JF) graded the OCT scan. This allowed to minimize inter-observer variation.

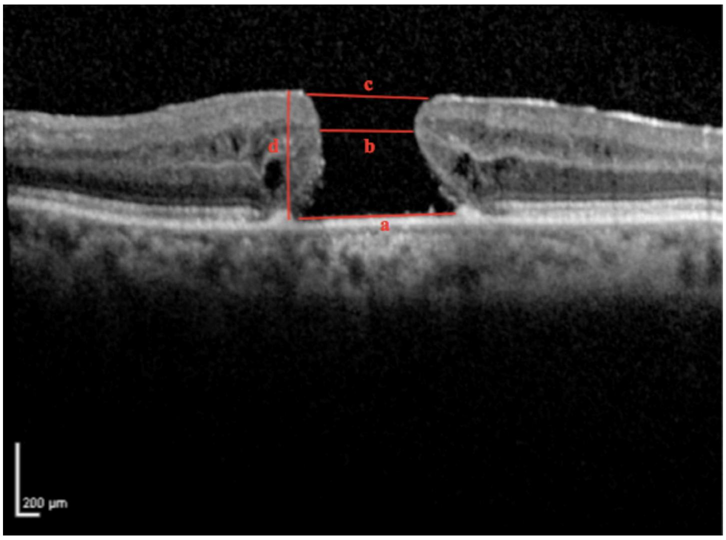


Figure 1: Spectralis SD – OCT preoperative scan measurements - (a) base diameter; (b) minimum diameter; (c) inner opening diameter; (d) hole height. MHI=d/a.

For statistical analysis, STATA 14® (StataCorp LLC) was used. Categorical or binary data was described using absolute counts and percentages. Ordinal data was further described using the median and interquartile range. Continuous measurements were described using the mean and standard deviation, after checking for normality visually using histograms and statistically using the Shapiro-Wilk test. For inferential statistics, paired t-tests were used for visual acuity analysis. Univariate logistic and linear regression was used to determine predictors of closure and visual acuity, respectively. A two-sided significance level of 5% was considered.

Results

We included 44 patients (44 eyes), of which 26 patients were women (59,1%), with a mean age of 66,9±9,8 years. Mean follow-up was 81,8±23,4 months and mean baseline BCVA was 36,2±13,4 letters (approximately 20/200±20/500 in ETDRS Equivalent Snellen Fraction) (minimum 20, maximum 65 letters) (Table 2). Involvement of the fellow eye with vitreoretinal interface disease (VMT and/or full-thickness macular hole) was identified in 13 patients (29,6%) previous and/or during follow-up.

Before surgery, only 3 patients (6,8%) were pseudophakic; 10 patients (22,7%) underwent phacoemulsification simultaneous with vitrectomy for macular hole repair. At the end of follow-up, 31 patients (70,5%) were pseudophakic. Regarding vitrectomy technique, simple ILM peeling was used in all but one case where the inverted ILM flap technique was employed.

Table 2: Assessment of baseline demographic variables

Age, years (mean±SD, min-max)	66,9 ± 9,8	(35-84)
Female (n, %)	26	(59,1%)
Left eye (n, %)	23	(52,3%)
Follow-up, months (mean±SD, min-max)	81,8 ± 23,4	(55-128)
Baseline BCVA (mean±SD, min-max)	36,2 ± 13,4	(20 - 65)

According to Gass' classification, the majority of the 44 patients (90,9%) had a stage 3 or stage 4 MH: 16 had a stage 3 MH (36,4%) and 24 (54,6%) patients had a stage 4 MH. Forty-two patients (95,5%) had a full-thickness macular hole regardless the size without VMT in IVTS classification. From Uchino's classification 17 patients (38,6%) had a stage 3 MH and 24 had a stage 4 MH. The majority MH size was above 400 μm (32 patients – 76,2%). In baseline OCT scans were found CME, ERM and EPRP in 28 (63,6%), 12 (27,3%) and 8 (18,2%) patients, respectively (Table 3).

Table 3: Status of vitreo-retinal interface at baseline.

Gass 1/2/3/4 (n, %)	1 (2,3%)/ 3 (6,8%)/ 16 (36,4%)/ 24 (54,6%)	
IVTS - equivalent Gass stages 3/4 (n, %)	2 (4,55%)/ 42 (95,45%)	
Uchino 2/3/4 (n, %)	3 (6,8%)/ 17 (38,6%)/ 24 (54,6%)	
MH size (n, %)		
<250	2	(4,5%)
250-400	9	(20,5%)
>400	33	(75%)
CME (n, %)	28	(63,6%)
ERM (n, %)	12	(27,3%)
EPRP (n, %)	8	(18,2%)

CME: cystoid macular edema; EPRP: epiretinal proliferation; ERM: epiretinal membrane; MH: macular hole.

The mean results obtained from the measurement of macular holes' base diameter, inner opening diameter, minimum linear diameter, MH height, MHI and CMT are presented in Table 4.

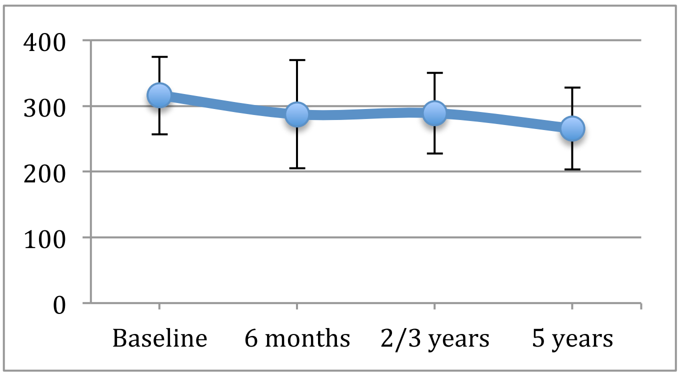
Table 4: Baseline MH measures

Base diameter (mean±SD, min-max)	1069,77 ± 324,98	(160 - 1863)
Inner opening diameter (mean±SD, min-max)	853,39 ± 248,85	(320 - 1243)
Minimum linear diameter (mean±SD, min-max)	514,95 ± 194,19	(88 - 882)
MH height (mean±SD, min-max)	392,91 ± 92,92	(188 - 581)
MHI (mean±SD)	0,41 ± 0,20	
CMT (mean±SD, min-max)	315,89 ± 59,29	(200 - 432)

CMT: central macular thickness; MH: macular hole; MHI: macular hole index; MHI=MH height/base diameter.

In the postoperative period, the mean CMT at 6 months, 2/3 years and 5 years was 287,28±82,48 µm, 289,08±61,38 µm and 265,9±62,42 µm, respectively. Figure 2 show the mean CMT variation along time course of follow-up. CMT significantly decreased with follow-up, with a reduction of -37,1±83,9 µm at 6 months (p=0.037) and -50,0±80,3 µm at 5 years (p<0.001). There is a non-significant reduction of CMT from 6 months to 5 years (-19,55±15,76 µm, p=0.23, n=25).

Figure 2: Changes in CMT after surgery, comparing with baseline. Data represent mean ± standard deviation (SD).



At early 6 months only 2 holes remained open (success rate for macular closre was 96% immediatly after vitrectomy). At 2/3 years 1 of these holes closed spontaneously and another 2 patients had recurrence of the hole, making a total of 3 MH at this time of follow-up. At the end of 5 years follow-up MH closure was achieved in 40 patients (90,9%). The 4 patients who did not achieve anatomic closure at 5 years of follow-up are characterized in Table 5. Only 1 of these patients had a hole that never closed during the follow-up period. Due to the low number of events (4 out of 44), inferential statistical analysis regarding predictors of closure was not carried out.

Table 5: Persistent macular holes at 5 years

Patient	Age	Sex	Primary closure after vitrectomy	Gass/ IVTS/ Uchino's stages	MH size	Baseline EDTRS	5 Years EDTRS
1	62	Male	Yes	4/4/4	1030 µm	35,00	19,95
2	86	Female	Yes	4/4/4	872 µm	19,95	35,00
3	43	Male	Yes	3/4/3	415 µm	35,00	50,05
4	70	Female	No	3/4/3	640 µm	19,95	30,15

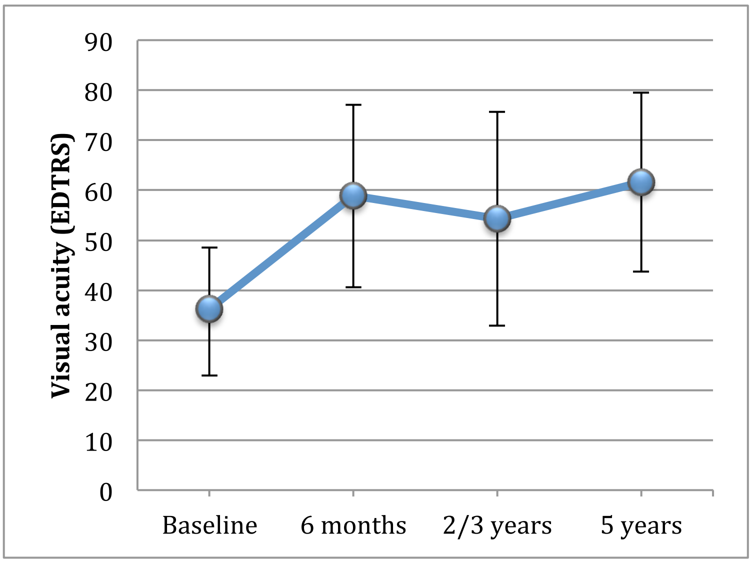
At the early 6 months, 2/3 years and 5 years OCT scans, we found that 2, 3 and 3 patients (including closures and non-closures), respectively, had CME.

Post-operative cohort mean BCVA at 6 months, 3 years and 5 years of follow-up was 58,84±18,29 (approximately 20/63±20/400 in ETDRS Equivalent Snellen Fraction), 54,3±21,44 (approximately 20/80±20/400 in ETDRS Equivalent Snellen Fraction) and 61,61±17,89 (approximately 20/60±20/500 in Snellen Fraction) letters, respectively (Table 6). BCVA variation (versus baseline) at 6 months, 3 years and 5 years was 21,21±16,1, 16,00±25,68 and 25,38±18,53 respectively; these differences are statistically significant in all timepoints ($p<0.001$) demonstrating improved visual acuity that is maintained at 5 years of follow-up. At 2/3 years of follow-up, there seems to be a decrease in visual acuity (comparing with BCVA at early 6 months), however only 30 patients were evaluated at this time point. These visual outcomes are summarized in Table 6 and Figure 3. BCVA variation (versus 6 months) at 5 years was 5,03±12,05 EDTRS letters and this difference was statistically significant ($p=0,025$), also demonstrating improved visual acuity that is maintained at 5 years of follow-up. However, only 32 patients were evaluated.

Table 6: Difference from baseline

	Baseline	Early 6 months	Mid 2-3 years	Last 5 years
Mean EDTRS (mean±SD, min-max)	36,2±13,4 (20-65)	58,84±18,29 (20-85)	54,3±21,44 (20-85)	61,61±17,89 (20-85)
VA differences (mean±SD)	-	21,22±16,1	16±25,68	25,38±18,53

Figure 3: Changes in BCVA after surgery, comparing with baseline. Data represent mean ± standard deviation (SD).



At the end of the 5 years of follow-up, two of the patients (4,6%) had a visual acuity decrease of more than 5 letters, 4 (9,1%) maintained visual acuity (within five letters of baseline BCVA) and the large majority, 38 (86,4%) had visual acuity gains over 1 line (>5 letters) (Figure 4).

The two patients who had a visual acuity decrease remained phakic, those who maintained visual acuity did not.

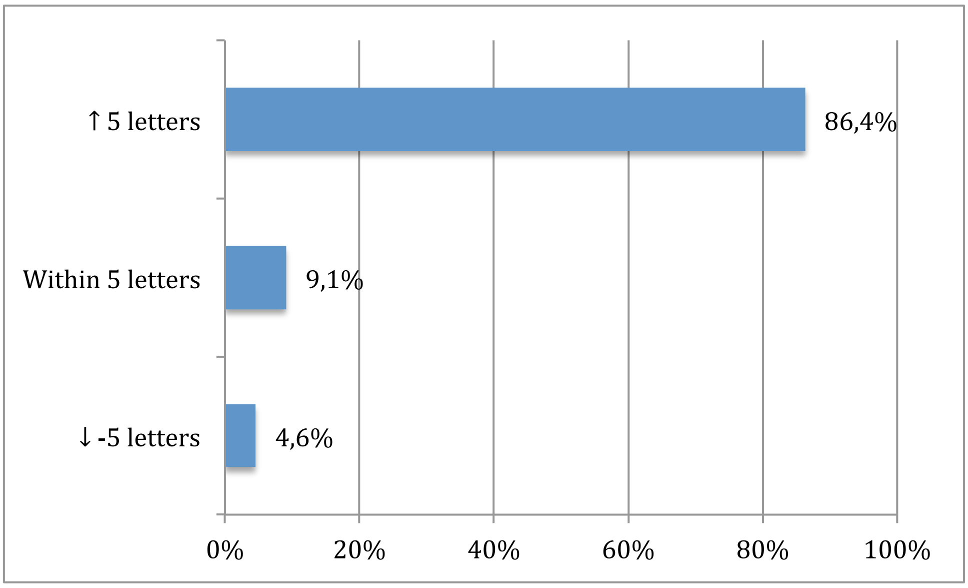


Figure 4: Distribution of visual acuity outcomes at the end of follow-up.

Neither demographic variables, holes' stages or OCT parameters, such as base diameter, inner opening diameter, minimum linear diameter, MH height, CMT and MHI, were found to be significantly associated with BCVA at the end of follow-up in univariate linear regression analysis (all $p>0.05$). Furthermore, at the end of follow-up, visual acuity improvement did not differ by lens status (pseudophakic +24.3±16.4 letters vs phakic +27.9±23.4 letters, $p=0.563$).

Discussion

Patients' mean age is similar to that of others studies conducted[1,4,11,13,19,20] as the involvement of the gender, which was superior in women. Ezra *et al* affirmed that although most patients at the time of diagnosis have idiopathic macular hole in only one eye, 0 to 29% of patients have an increased risk of developing bilateral MH[20], as it was possible to verify in this study, with bilateral MH in 29.6% (n=13) of the cases previous and/or during follow-up.

At 6 months of follow-up just 2 of the patients had persistent macular hole, so the anatomical success at this time point was high. At early 6 months Wakely *et al*[5], obtained a percentage of closure lower (84,0%) than that of our study and they did not obtain such good results in the BCVA variation.

Hirokazu Sakaguchi *et al*[16] had shown on their 5 years follow-up study that visual acuity improvement has its limitations if macular complications occur, as it could be verified by the occurrence of CME or cataract. However, in our study, at the end of follow-up, visual acuity improvement did not differ by lens status.

Analysing the time-course changes in BCVA for consecutive MH cases, our study suggested the possibility of gradual improvement in visual function, which is in accordance with what Sakaguchi *et al*[16] and Purtskhvanidze *et al*[13] had shown (Table 7). H. Sakaguchi *et al*[16] and K. Purtskhavanidze[13] *et al* obtained a better improvement than this study, which may also be explained by the higher rates of anatomical success. H.Sakaguchi *et al*[16] also evaluated the mean BCVA variation between 6 months and 5 years, obtaining better results (0,18 in LogMAR) than our study during this time of follow-up, given that only 32 of the 44 patients in the current study had visual acuity assessments at these two time points for comparison and analysis. Albeit with worse results, this difference was statistically significant, meaning there is a real gain in BCVA along this time frame.

Table 7: Comparison with other studies

Studies	N	Average Follow-up (months)	Mean BCVA variation (logMAR)	Closed MH % after 1 surgery
Our case-series	44	81,8 ± 23,4	1,19±1,33	90,9
H. Sakaguchi (2012)	20	83,4 ± 10,5	(Baseline: 0,73; Final:0,12)	95,7
K. Purtskhvanidze (2013)	51	54,0 ± 20,0	(Baseline: 0,70 ± 0,30; Final: 0,14 ± 0,10)	100,0

The highest gain was obtained between baseline and 6 months (Figure 3), which would be expected according to available studies.[1,18] Although the largest increase was between baseline and 6 months, the highest BCVA was achieved at the last follow-up. Overall, in this study, at the end of the 5 years of follow-up and comparing with baseline, 38 patients (86,4%) had a visual acuity gain greater than 1 line (>5 letters) and only 2 patients had a decrease in BCVA, one of the cases being a non-closure MH. As previously mentioned, only 2 patients had loss of visual acuity from baseline; both patients were phakic at the last follow-up evaluation, so visually significant cataract might have been a factor in these cases.

Despite the improvement of visual acuity, there is a significant number of patients who have missing data at 2/3 years, which is why the BCVA seems to worsen at this time point and this is a shortcoming in this study that should be addressed in future studies using a prospective data collection design.

Wakely *et al*[5] indicated that there is no real advantage to be gained by calculating derived indices from the basic ophthalmic measurements, however, to our knowledge, this study is the first to set the 5 years' anatomical and visual outcomes, resorting to OCT scans and holes measurements, before and after surgery and to know the rate of macular hole's reopening, as well as predictors of good or bad prognosis.

Considering the need for an OCT scan for an accurate representation of anatomical success, once it was available it became an essential tool to assess hole measurements and to predict good surgical outcomes.[5] In view of this, many authors have described different methods of macular hole measurements and compare some of these to try to regress them against anatomical and visual outcomes. Namely, some studies, although with shorter follow-up periods, have shown that the recovery of the external limiting membrane and photoreceptor inner-outer segment junction line are related to functional recovery after MH surgery.[19,21,22]

Albeit with a shorter follow-up period and a relatively small percentage of anatomical success, Wakely *et al*[5] had shown that the preoperative base diameter, macular hole inner opening and minimum linear diameter were associated with both anatomical and visual success. This can probably be explained by the number of non-closures and the shorter period of the study (5,36 ± 2,27 months) which includes the period of recovery of the retinal layers which could be slow and can be extended over the years[1].

In contrast with that, Purtskhvanidze *et al*[13], which has a similar mean follow-up time course, did not find a correlation of MH size and the final BCVA and they say this can be explained probably because they included only MH successfully closed. This is in accordance with our study, which has similar, although lower, closure rates (Table 7). Still, postoperatively, they found that central macular thickness gradually decreased, as in our study, with CMT thinner at 5 years (Figure 2). Nevertheless it does not seem to correspond to a real macular atrophy, because there is a functional improvement over the follow-up period (Figure 3), as also Purtskhvanidze *et al*[13] referred. With this, we cannot exclude further postoperative decrease of CMT after the follow-up period of this study.

Therefore, in descriptive terms, there is a reduction of the CMT during the follow-up period, as well as between the 6 months and 5 years, but that did not prove to be significant. As mentioned above, for this analysis, only 25 of the patients presented CMT values for these moments of follow-up, which becomes a limitation of the study.

Despite what has been said previously, we could not identify factors of good or bad prognosis, since closure rate was very high, thus impeding inferential statistics on that regard on only 4 non-closure cases.

The main limitation of this study is its retrospective design, which explains missing data at some time points. However, retrospective designs are useful for their high feasability and hypothesis-generating possibilities. In addition, the fact that vitrectomy has been performed by several surgeons is also another limitation.

Overall, albeit with a small sample, the patients involved in the present study obtained a BCVA that improved postoperatively throughout the follow-up period, reaching good levels in most patients. This improvement was correlated with anatomical success and few post-vitrectomy complications, which is in agreement with the results obtained in other studies.[3,11,16]

Hereupon, future prospective studies evaluating long-term outcomes in macular holes should be conducted to confirm our preliminary evidence of long-term functional and structural improvement.

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