Clinical characteristics of full thickness macular holes that closed without surgery

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ABSTRACT

Purpose To ascertain the anatomic factors that help achieve non-surgical sealing in full thickness macular hole (FTMH).

Methods Retrospective collaborative study of FTMH that closed without surgical intervention.

Results A total of 78 patients (mean age 57.9 years) included 18 patients with blunt ocular trauma, 18 patients that received topical or intravitreal therapies and 42 patients with idiopathic FTMH. Mean±SD of the initial corrected visual acuity (VA) in logMAR improved from 0.65±0.54 to 0.34±0.45 ($p<0.001$) at a mean follow-up of 33.8±37.1 months. FTMH reopened in seven eyes (9.0%) after a mean of 8.6 months. Vitreomacular traction was noted in 12 eyes (15.8%), perifoveal posterior vitreous detachment in 42 (53.8%), foveal epiretinal membrane in 10 (12.8%), cystoid macular oedema (CME) in 49 (62.8%) and subretinal fluid (SRF) in 20 (25.6%). By multivariate analysis, initial VA correlated to the height ($p<0.001$) and narrowest diameter of the hole ($p<0.001$) while final VA correlated to the basal diameter ($p<0.001$). Time for closure of FTMH (median 2.8 months) correlated to the narrowest diameter ($p<0.001$) and the presence of SRF ($p=0.001$). Mean time for closure (in months) was 1.6 for eyes with trauma, 4.3 for eyes without trauma but with therapy for CME, 4.4 for eyes without trauma and without therapy in less than 200 µm in size and 24.7 for more than 200 µm.

Conclusion Our data suggest an observation period in new onset FTMH for non-surgical closure, in the setting of trauma, treatment of CME and size <200 µm.

INTRODUCTION

Full thickness macular hole (FTMH) is a relatively uncommon ocular disease.[1] However, it is commonly encountered by retina specialists and is commonly treated with vitrectomy, fluid-gas exchange, internal limiting membrane peel, and in lower prognosis cases, with internal limiting membrane flap techniques, foveoplasty manoeuvres, retinal[2] or amniotic membrane graft placement.[3] Several reports indicate a subset of FTMH may close without surgical intervention in a small percentage.[4–10]

To characterise some of the variables that lead to non-surgical hole closure, we collected retrospectively in a collaborative manner the largest series of FTMH cases that closed without surgical intervention.

MATERIALS AND METHODS

An open invitation for the contribution of cases from retina specialists wishing to participate was announced by email worldwide using several of the authors network. A standardised data collection sheet was distributed to all collaborators from 1 January 2019 to 31 December 2020.

Cases with established diagnosis of FTMH by spectral domain optical coherence tomography (SD-OCT) that sealed on follow-up without surgical intervention were collected retrospectively. The closure of FTMH was defined as a flattened and reattached hole rim along the whole circumference of the hole or type 1 closure (absence of foveal neurosensory retinal defect).[11] Inclusion criteria included traumatic or idiopathic, acute or chronic FTMH of all ages, gender or racial backgrounds. Exclusion criteria included retinal dystrophy, foveoschisis, neovascular age-related macular degeneration and a history of vitreous surgery of less than 1 year or phacoemulsification of less than 6 months prior to diagnosis of FTMH. Eyes with poor SD-OCT quality were excluded. In case the closure of FTMH was suspected to be incomplete,

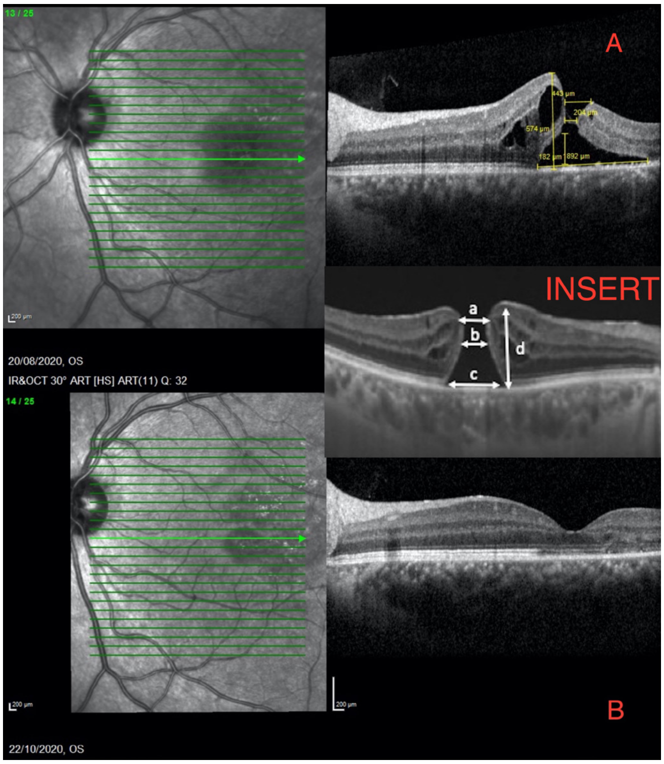

Figure 1 Full thickness macular hole parameters noted in the insert (height=d, apical diameter=a, minimum diameter=b, basal diameter=c). Spectral domain optical coherence tomography scans of the left eye before (A) and 2 months after closure (B) with a total of 4 months follow-up. This 24-year-old Caucasian man sustained sport injury and was started on topical non-steroidal anti-inflammatory drug. Visual acuity improved from 6/12 (20/40) to 6/6 (20/20).

additional oblique cuts were requested. Previously published cases were also excluded. Corrected visual acuity (VA) was recorded as Snellen vision and converted to log MAR.

Two masked reviewers (SHU and AM) independently screened the SD-OCT images for inclusion. FTMH parameters were measured using Image J by one of us (SHU) in order to correct for differences in SD-OCT machines. Macular parameters included height, basal diameter, apical diameter and narrowest diameter (figure 1). In addition, FTMH parameters were calculated such as height/basal diameter or Macular Hole Index (MHI), narrowest diameter/basal diameter or Diameter Hole Index (DHI) (indicator of tangential traction), height/narrowest diameter or Tractional Hole Index (THI) (indicator of anteroposterior traction and retinal hydration) and volume of the subretinal fluid (SRF) ($\pi/24\times H\times(BD^2+ND^2+BD\times ND)$) (H, height; BD, basal diameter; ND, narrowest diameter).[12]

Statistical analysis was performed using SPSS software V.26 (SPSS). Descriptive statistics were computed (table 1). One-tailed t-test with equal variances not assumed was done for subgroup analyses. One-way analysis of variance was applied for continuous variables and χ^2 test for the difference between proportions for categorical binomial variables, when comparing the four subgroups (trauma with therapy, trauma without therapy, no trauma no therapy and no trauma with therapy) (table 2). P values of less than 0.05 were considered statistically significant. Two types of multivariate analysis were used: (1) discriminant analysis for the dependent variables perifoveal posterior vitreous detachment (PVD), epiretinal membrane (ERM), cystoid macular oedema (CME), SRF; (2) multiple linear analysis for the

Table 1 Clinical data on 78 patients with non-surgical sealing of full-thickness macular holes

Characteristic	Data
No. of patients	78
Male gender N (%)	47 (60.3)
Caucasian N (%)	72 (92.3)
Blunt ocular trauma N (%)	18 (23.1)
Therapy for CME	
Topical corticosteroid	13 (16.7)
Topical NSAID	7 (9.0)
Intravitreal VEGF antagonists	4 (10.3)
Age (years) range N (%)	
<20	7 (9.0)
21–40	9 (11.5)
41–60	11 (14.1)
61–70	29 (37.2)
>70	22 (28.2)
Right eye N (%)	36 (46.2)
Spherical equivalent (dioptre) N (%) before cataract surgery	
+4.00 to emmetropia	31 (39.7)
−0.25 to −2.00	27 (34.6)
−2.25 to −6.00	8 (10.3)
Myopia >6.00	5 (6.4)
NA	7 (9.0)
Pseudophakic, no. (%)	20 (25.6)
FTMH height (µm)	
<100	22 (28.2)
100–199	32 (41.0)
200–299	14 (17.9)
>300	10 (12.8)
FTMH basal diameter (µm)	
1–200	18 (23.1)
201–500	25 (32.1)
501–1000	20 (25.6)
>1000	15 (19.2)
FTMH apical diameter (µm)	
<300	16 (20.5)
300–499	38 (48.7)
>500	24 (30.8)
FTMH narrowest diameter (µm)	
0–100	25 (32.0)
101–200	29 (37.2)
>200	24 (30.8)
MHI (height/basal diameter)	1.00±0.78
DHI (narrowest diameter/basal diameter)	0.39±0.24
THI (height/narrowest diameter)	2.67±1.44
SRF volume (10^7) μm^3	12.0±42.4
Initial VA (log MAR)	0.65±0.54
Final VA (log MAR)	0.34±0.45
VA gain (log MAR)	
Visual loss	4 (5.1)
0	12 (15.8)
0–0.2	19 (24.4)
0.21–0.4	21 (26.9)
0.41–0.6	11 (14.1)
>0.6	11 (14.1)
Follow-up (months)	33.8±37.1
Time to FTMH closure (months)	

Continued

Table 1 Continued

Characteristic	Data
0–1	22 (28.2)
2–3	23 (29.5)
4–6	16 (20.5)
>6	15 (19.2)
NA	2 (2.6)

The values listed in the right column refer to either mean±SD or values (percentage).
CME, cystoid macular oedema; D, dioptres; DHI, Diameter Hole Index; FTMH, full thickness macular hole; MHI, Macular Hole Index; NA, not assessed; NSAID, non-steroidal anti-inflammatory drug; SRF, subretinal fluid; THI, Tractional Hole Index; VA, corrected visual acuity; VEGF, vascular endothelial growth factor.

dependent variables height, basal diameter, narrowest diameter, MHI, DHI and THI.

RESULTS

A total of 78 patients diagnosed with FTMH had a mean age of 57.9 years and included 18 patients with blunt ocular trauma and 18 patients that received topical or intravitreal therapies. There was a male preponderance with 47 men and 31 women (table 1). Racial distribution comprised 72 Caucasians, 3 Asian Indians, 2 African Americans and 1 Asian. Systemic diseases included diabetes mellitus in eight patients. Blunt trauma occurred in 18 patients including 8 with sport injury (figures 1 and 2). Laterality included 36 right eyes and 42 left eyes. Mean refractive error was −1.5±4.0 dioptre (median −0.5; range −23 to +3.75 dioptre), including four patients with high myopia (−9 to –12, −15 and −23 dioptre).

The patients were in three categories those who were awaiting surgery, or those who denied surgery and returned with improved vision, and those who were placed on initial observation (in the traumatic category). Ocular medical history included four primary open angle glaucoma, two dry form of age-related macular degeneration, two diabetic macular oedema, one preproliferative diabetic retinopathy, one proliferative diabetic retinopathy and one retinal vein occlusion. Past ocular surgical interventions included 20 cataract surgeries, 5 pars plana vitrectomies (for indications of vitreous haemorrhage or retinal detachment with vitrectomy performed more than 1 year prior to the diagnosis of FTMH), 1 trabeculectomy, 1 panretinal photocoagulation, 2 argon laser retinopexy for a horse-shoe tear, 1 scleral buckle, 1 laser-assisted in situ keratomileusis and 1 neodymium: Yttrium-Aluminium Garnet laser capsulotomy.

The mean time to closure after initial detection was 6.2±10.8 months (median 2.8; range 0.5–52 months) (figure 3). The mean log MAR initial corrected VA was 0.65±0.54 (20/89 or 6/27) (median 0.48; range 0–2.5) and improved to 0.34±0.45 (20/44 or 6/13) (median 0.18; range 0–2) ($p<0.001$) at the last mean follow-up of 33.8±37.1 months (median 16 months; range 1–157 months).

Vitreomacular traction (VMT) was noted in 12 (15.4%) eyes, PVD in 42 (53.8%), foveal ERM in 10 (12.8%), CME in 49 (62.8%) and SRF in 20 (25.6%) eyes by SD-OCT. The mean (±SD) dimensions measured were: FTMH height was 365.2±141.2 µm (median 333.5, range 167–856), basal diameter 688.2±727.8 µm (median 447.5, range 92–4732), apical diameter 423.3±162.2 µm (median 419.5, range 94–832) and narrowest diameter 174.7±102.5 µm (median 149.5, range 40–508).

FTMH closure was categorised as complete in 74 eyes with SRF or outer retinal defects persisting in two eyes each at the last follow-up examination. Non-surgical therapy offered when FTMH was detected was implemented in 18 patients: 4 received intravitreal vascular endothelium growth factor (VEGF) antagonists, 13 received topical corticosteroid and 7 received topical non-steroidal anti-inflammatory drug (NSAID) (multiple in some). A total of four patients were receiving a topical prostaglandin analogue at initial examination, and in two of these four, FTMH closed 1–3 months after discontinuation of medication.

The initially closed FTMH reopened in seven eyes (9.0%) after a mean of 8.6 months distributed at 3, 4 (two eyes), 5, 6, 16 and 22 months. Among the seven eyes that reopened, two closed after vitrectomy, one stayed open after vitrectomy and one closed on topical corticosteroid and topical NSAID. No surgery was performed in four eyes. A total of 74 eyes had stable or improved final vision while four eyes lost vision from

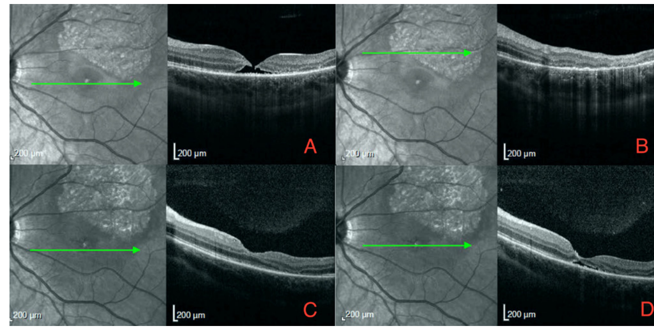

Figure 2 Spectral domain optical coherence tomography scans of the left eye before (A, B) and after spontaneous self-closure (C, D) during the 1 month of observation in a 19-year-old Caucasian woman who sustained a sport injury to the left eye. Visual acuity improved from 6/45 (20/150) to 6/9 (20/30). Commotio retina is noted on presentation superior to the full thickness macular hole (B).

Table 2 Eyes with full thickness macular hole were divided into four groups according to presence of blunt ocular trauma and non-surgical ocular therapies with p value based on one-way analysis of variance ANOVA

Category	Trauma no therapy	Trauma with Therapy	No trauma no therapy	No trauma with therapy	P value
Number	10	8	50	10	
Age (year)	23.4±9.7	25.1±10.5	68.3±8.3	66.7±9.1	
Time to closure (months)	1.6±0.8	1.7±1.2	8.1±12.9	4.3±3.8	0.18
Initial VA	0.94±0.50	1.03±0.79	0.45±0.38	0.64±0.50	0.001
Final VA	0.57±0.66	0.50±0.65	0.21±0.22	0.43±0.56	0.029
Visual gain	0.37±0.47	0.54±0.35	0.24±0.33	0.21±0.17	0.10
PVD N (%)	0 (0%)	0 (0%)	34 (68%)	8 (80%)	<0.001
ERM	0 (0%)	0 (0%)	5 (10%)	5 (50%)	0.002
CME	4 (40%)	3 (38%)	33 (66%)	9 (90%)	0.05
SRF	7 (70%)	7 (88%)	4 (8%)	2 (20%)	<0.001
Height (µm)	297±141	460±192	351±111	426±192	0.036
Basal diameter (µm)	993±326	1937±1379	421±333	723±675	<0.001
Apical diameter (µm)	524±185	480±164	392±162	436±80	0.08
Narrowest diameter (µm)	256±112	233±93	152±85	162±133	0.007

CME, cystoid macular oedema; ERM, epiretinal membrane; PVD, posterior vitreous detachment; SRF, subretinal fluid; VA, corrected visual acuity.

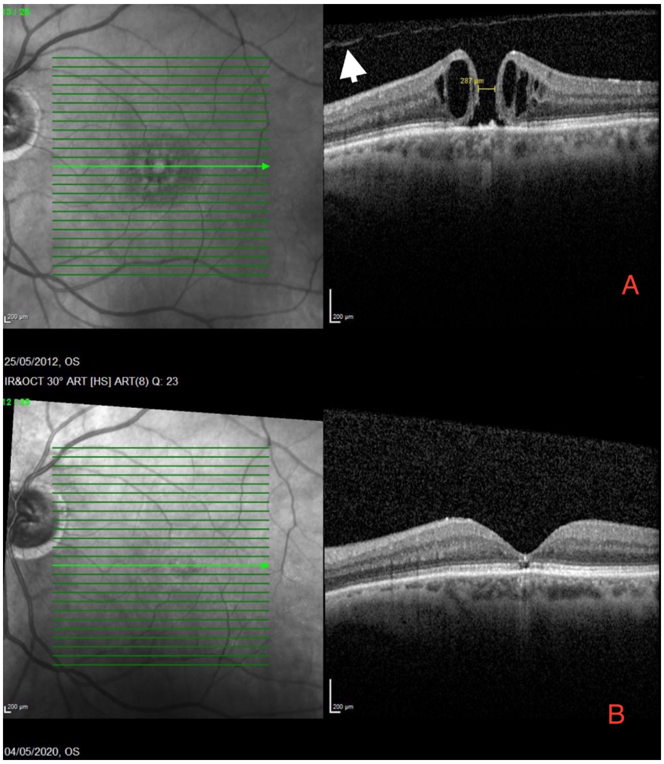

Figure 3 Spectral domain optical coherence tomography scans of the left eye before (A) and after self-closure (B) in a 75-year-old healthy pseudo-phakic Caucasian man. Visual acuity improved from finger counting to 6/60 (20/200). Patient received no topical therapy for cystoid macular oedema. No history of ocular trauma or systemic medications. Note the perifoveal posterior vitreous detachment (arrow). The closure time was 45 months.

foveal scar after blunt trauma (two eyes) and from foveal retinal pigment epithelium atrophy (two eyes). Three FTMH resolved after resolution of the VMT and three FTMH closed after new occurrence of PVD (two of three having VMT). One FTMH closed despite persistence of the VMT.

Comparing the traumatic FTMH group to the non-traumatic without therapy group revealed (table 2): younger age (24.2 vs 68.3; p<0.001), shorter time to closure (1.6 vs 8.1 months; p=0.001), worse initial VA (0.98 (20/191 or 6/57) vs 0.45 (20/56 or 6/17); p=0.003), additional visual gain of two lines (0.44 vs 0.24 logMAR; p=0.038), difference in perifoveal PVD (0% vs 68%; p<0.001), wider basal diameter (1412 vs 421 µm; p=0.001), wider apical diameter (504 vs 392 µm; p=0.025) and wider narrowest diameter (246 vs 152 µm; p=0.001). Traumatic FTMH did not differ between eyes that received therapy and those not receiving any non-surgical therapy for time of closure (p=0.80) or visual gain (p=0.40). Visual gain was not different between eyes with non-traumatic FTMH without therapy and eyes in the non-traumatic FTMH receiving therapy (0.24 vs 0.21 logMAR; p=0.35) while time for closure was longer in the non-traumatic without therapy vs the non-traumatic with therapy (8.1 vs 4.3 months; p=0.045). Note that the presence of CME in the non-traumatic treated group was 90% versus 66% in the non-traumatic without treatment group.

When the narrowest diameter of non-traumatic non-therapy FTMH was less than 200 µm, the mean time to closure was 4.4 months versus a mean of 24.7 months if the size was above 200 µm (p<0.001). The mean time to closure was 4.3 months in non-traumatic FTMH on therapy. Perifoveal PVD was associated with longer time of closure when all 78 eyes were analysed (p=0.001). In eyes without trauma, the time for closure was marginally less when perifoveal PVD was absent (4.6 months) than when perifoveal PVD was present (8.7 months) (p=0.12). In eyes without trauma and without therapy, the closure time was marginally longer in eyes with CME (8.2 months) than in eyes without CME (5.8 months) (p=0.24).

Using the partial regression coefficients (slopes) of the multivariate analysis between the independent variables (age, trauma, therapy, VA and time for FTMH closure) and the dependent variables (FTMH parameters) revealed the following: perifoveal PVD (p<0.001), ERM (p=0.007), CME (p=0.018) and height (p<0.001) correlated positively with increasing age. Similarly, the narrowest diameter correlated positively with trauma (p=0.003), initial VA and time for closure. The initial VA correlated positively with FTMH height (p<0.001) and narrowest diameter (p<0.001) while final VA correlated to basal diameter (p<0.001). Time for FTMH closure correlated to narrowest diameter (p<0.001) and presence of SRF (p=0.001). MHI negatively correlated with age (p=0.002) while THI negatively correlated with age (p<0.001) and time for closure (p=0.002).

DISCUSSION

The current study, a retrospective multicentre collaborative study, corroborates the entity of non-surgical sealing of FTMH and suggest that it may be appropriate to observe a selected FTMH to allow for closure such as small, trauma-induced, or those with cystic characteristics under treatment. Periodic re-examination and following with serial OCT can reveal progressive narrowing and subsequent closure of FTMH, thus potentially avoiding the need for surgical intervention; enlarging FTMH are more clearly candidates for prompt vitrectomy.[4]

Spontaneous and speedy closure of traumatic FTMH has been reported to be associated with younger age, and smaller hole size.[5–10 13–21] We found that all traumatic FTMH that closed lacked PVD and sealed by a mean of 1.6 months regardless of FTMH size. Hypotheses as to why this might be the case include more vigorous fibro-cellular proliferation (to bridge the gap) or more formed vitreous (to guide bridging cells and prevent hydration of the macular hole edges) in young patients. Miller *et al*[14] followed 11 traumatic macular holes that closed a median 5.7 weeks and found a trend for a smaller size in the self-sealing group compared with a control group of FTMH that initially underwent vitrectomy. A multicentre prospective comparative study of observation (15 patients) versus vitrectomy (25 patients) in a selected cohort yielded a closure rate of 66.7% in the observational group (median closure of 2.5 months) and 100% for the surgical group.[21]

A second entity that may be associated with non-surgical closure is CME-associated FTMH,[18–20] perhaps especially when treated by topical corticosteroids, topical NSAID or intravitreal VEGF antagonists. Niffenegger *et al*[19] described eight patients (nine eyes with FTMH and CME) who received either difluprednate with a topical carbonic anhydrase inhibitor or topical NSAID. Eight eyes (89%) achieved hole closure with resolution of CME and visual improvement after a mean of 6 weeks of therapy. Sokol *et al*[18] described 14 patients with FTMH and CME that underwent successful topical medical treatment for a mean period of 5.6 weeks, with half of the patients having had prior vitrectomy. Elhusseiny *et al*[15] hypothesised that CME facilitates spontaneous closure by approximating the edges, a form of healing by primary intention. In the current series with CME and absence of trauma, there was a significantly faster closure of FTMH in the therapy arm (4.3 months) than in the no therapy arm (8.1 months).

FTMH self-closure, like surgical closure, in adults has been hypothesised to result from cell proliferation at the base of the hole,[7] formation of a contractile ERM resulting in shrinkage and closure of the hole,[16] and complete detachment of the posterior hyaloid from the foveal area (perifoveal PVD) resulting in the release of an anteroposterior traction.[17] Closure with resolution of the VMT and PVD formation in some eyes in the current study are consistent with the latter hypothesis. In a different perspective, we found a marginally faster closure time in non-traumatic no therapy eyes without PVD than with eyes with PVD hence the role of sandwiching the active cellular elements at the base of the hole. Of note is that there were eight patients with epithelial proliferation noted on the edges of the holes, similar to that seen in non-tractional lamellar holes (LHEP or that lamellar hole epiretinal proliferation). LHEP was still evident after the holes closed. In addition, four patients developed LHEP after hole closure.

Guyer *et al*[16] reported resolution of the FTMH in 3 (5%) of 66 patients followed for a mean of 4.7 years without any sign of hole by funduscopy, although before the era of OCT. Yuzawa *et al*[22] in their study showed that among 97 eyes with FTMH planned for surgery, the spontaneous FTMH closure was observed in six cases (6.2%). Sugiyama *et al*[10] reported the spontaneous macular hole closure in 5 (3.5%) of 142 eyes waiting for vitrectomy and in all of these 5 eyes the baseline macular hole diameter was less than 250 µm. Elhusseiny *et al*[15] described three cases of CME and FTMH that sealed spontaneously and reopened and closed a second time. A case with multiple spontaneous opening and closure of a myopic FTMH was reported by Golan and Barak.[23] In our series, the initially closed FTMH reopened in seven eyes (9.0%) after a mean of 8.6 months, hence, the need to observe for a minimum of 1 year all eyes who had non-surgical sealing of FTMH.

The mechanism of non-surgical sealing of FTMH is likely multifactorial: release of vitreoretinal interface forces, contraction of Müller cells,[7] formation of a fibrin plug,[20] inflammatory cells, or a bridge of ERM covering the hole and then shrinking, pulling the edges of the hole together. In case of FTMH associated with CME, the swelling resolves with therapy, the 'drawbridge closes'[20] allowing re-approximation of the inner retinal structures.

Limitations of our study include its retrospective design, the lack of comprehensive data regarding the exact onset of FTMH duration in some cases (excluding traumatic aetiology), the short follow-up and potential referral bias (incomplete data on the reasons behind halting surgery on most patients). For FTMH that are not showing signs of spontaneous closure, vitrectomy is clearly associated with better visual and anatomic outcomes compared with observation according to a recent meta-analysis.[24]

In conclusion, our data suggest that is reasonable to observe recent onset macular holes for non-surgical closure, particularly in the setting of blunt ocular trauma. In the setting of associated CME, a trial of non-surgical therapy and frequent periodic observation should be considered and offered to the patient as an alternative to early surgical intervention. This also applies for idiopathic FTMH without CME and with hole size less than 200 µm.

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Patient consent for publication Not required.

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REFERENCES

1 McCannel CA, Ensminger JL, Diehl NN, *et al*. Population-Based incidence of macular holes. *Ophthalmology* 2009;116:1366–9.
2 Rizzo S, Caporossi T, Tartaro R, *et al*. A human amniotic membrane plug to promote retinal breaks repair and recurrent macular hole closure. *Retina* 2019;39:S95–103.
3 Grewal DS, Mahmoud TH. Autologous neurosensory retinal free flap for closure of refractory myopic macular holes. *JAMA Ophthalmol* 2016;134:229–30.
4 Ohayon A, Rubowitz A. Spontaneous closure of bilateral macular holes. *Am J Ophthalmol Case Rep* 2019;15:100516.
5 Liu J, Peng J, Zhang Q, *et al*. Etiologies, characteristics, and management of pediatric macular hole. *Am J Ophthalmol* 2020;210:174–83.
6 Yamashita T, Uemara A, Uchino E, *et al*. Spontaneous closure of traumatic macular hole. *Am J Ophthalmol* 2002;133:230–5.
7 Bringmann A, Duncker T, Jochmann C, *et al*. Spontaneous closure of small full-thickness macular holes: presumed role of Müller cells. *Acta Ophthalmol* 2020;98:e447–56.
8 Chen H, Chen W, Zheng K, *et al*. Prediction of spontaneous closure of traumatic macular hole with spectral domain optical coherence tomography. *Sci Rep* 2015;5:12343.
9 Young LH, Mukai S, Vavvas DG. Long-Term follow-up and outcomes in traumatic macular holes. *Am J Ophthalmol* 2015;160:1255–8.
10 Sugiyama A, Imasawa M, Chiba T, *et al*. Reappraisal of spontaneous closure rate of idiopathic full-thickness macular holes. *Open Ophthalmol J* 2012;6:73–4.
11 Kang SW, Ahn K, Ham D-I. Types of macular hole closure and their clinical implications. *Br J Ophthalmol* 2003;87:1015–9.
12 Ruiz-Moreno JM, Staicu C, Piñero DP, *et al*. Optical coherence tomography predictive factors for macular hole surgery outcome. *Br J Ophthalmol* 2008;92:640–4.
13 Mitamura Y, Saito W, Ishida M, *et al*. Spontaneous closure of traumatic macular hole. *Retina* 2001;21:385–9.
14 Miller JB, Yonekawa Y, Eliott D, *et al*. Long-Term follow-up and outcomes in traumatic macular holes. *Am J Ophthalmol* 2015;160:1255–8.
15 Elhusseiny AM, Smiddy WE, Flynn HW, *et al*. Case series of recurring spontaneous closure of macular hole. *Case Rep Ophthalmol Med* 2019;2019:1–4.
16 Guyer DR, de Bustros S, Diener-West M, *et al*. Observations on patients with idiopathic macular holes and cysts. *Arch Ophthalmol* 1992;110:1264–8.
17 Preti RC, Zacharias LC, Cunha LP, *et al*. Spontaneous macular hole closure after posterior vitreous detachment in an eye with hyperreflective OCT stress line. *Am J Ophthalmol Case Rep* 2020;20:100950.
18 Sokol JT, Schechet SA, Komati R. Macular hole closure with medical therapy. *Opthalmology Retina* 2021. in press.
19 Niffenegger JH, Fong DS, Wong KL, *et al*. Treatment of secondary full-thickness macular holes with topical therapy. *Ophthalmol Retina* 2020;4:695–9.
20 Tornambe PE, genesis Mhole. The hydration theory. *Retina* 2003;23:421–4.
21 Chen H-J, Jin Y, Shen L-J, *et al*. Traumatic macular hole study: a multicenter comparative study between immediate vitrectomy and six-month observation for spontaneous closure. *Ann Transl Med* 2019;7:726.
22 Yuzawa M, Watanabe A, Takahashi Y, *et al*. Observation of idiopathic full-thickness macular holes. follow-up observation. *Arch Ophthalmol* 1994;112:1051–6.
23 Golan S, Barak A. Third time spontaneous closure of myopic macular hole. *Retin Cases Brief Rep* 2015;9:13–14.
24 Parravano M, Giansanti F, Eandi CM. Vitrectomy for idiopathic macular hole. *Cochrane Database Syst Rev* 2015;2015:CD009080.