FULL-THICKNESS MACULAR HOLE IN AGE-RELATED MACULAR DEGENERATION PATIENTS WITH TWO DISTINCT ENTITIES

A Multicenter Study

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Purpose: To describe optical coherence tomography characteristics of full-thickness macular holes (FTMHs) in age-related macular degeneration patients.

Methods: A multicenter, retrospective, observational case series of patients diagnosed with age-related macular degeneration and FTMHs seen between January 1, 2009, and January 3, 2020. Clinical charts and spectral-domain optical coherence tomography images were reviewed. Optical coherence tomography findings included FTMH-inverted trapezoid or hourglass appearance, central macular thickness (CMT), complete retinal pigment epithelium and complete retinal outer retinal atrophy, and presence of pigment epithelium detachment and epiretinal membrane. The mean outcome was the morphologic and functional characterization of different subtypes of FTMHs.

Results: A total of 86 eyes of 85 consecutive patients, with mean age of 80.31 ± 8.06 and mean best-corrected visual acuity of 1.17 ± 0.58 logarithm of the minimal angle of resolution. Two different subtypes of FTMHs were identified: tractional and degenerative. Fifty (58%) degenerative FTMHs characterized with inverted trapezoid appearance and 36 (42%) tractional FTMHs characterized with hourglass appearance. Degenerative FTMHs presented with 66% of CMT < 240 μm, 14% of CMT > 320, and 70% of complete retinal outer retinal atrophy, in comparison with 41% of CMT < 240 μm, 42.9% of CMT > 320%, and 20% of complete retinal outer retinal atrophy in the tractional FTMH group ($P = 0.002$, 0.003, <0.001, respectively). The presence of epiretinal membrane and pigment epithelium detachment where significantly higher in tractional FTMHs ($P = 0.02$, 0.03, respectively).

Conclusion: Degenerative and tractional FTMHs may be two distinct clinical entities. Discerning degenerative from tractional FTMHs is possible by using optical coherence tomography features including shape of the FTMHs, CMT, internal–external ratio of FTMHs, and presence of complete retinal outer retinal atrophy, pigment epithelium detachment, and epiretinal membrane.

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Age-related macular degeneration (AMD) is a leading cause of blindness and central vision loss worldwide. The hallmark of the neovascular AMD (NV-AMD) is choroidal neovascularization (CNV), whereas drusen, retinal, and choriocapillaris atrophy are the hallmarks of non-NV-AMD.[1,2]

A full-thickness macular hole (FTMH) is an anatomic opening of all the layers of the fovea featuring interruption of all neural retinal layers from the internal limiting membrane (ILM) to the retinal pigment epithelium (RPE).[3] Full-thickness macular holes are mostly idiopathic but can be secondary to highly myopic eyes or after ocular trauma.[4] Idiopathic FTMH prevalence is 0.3% of the population and almost never seen before the age of 55.[5] In 2013, The International Vitreomacular Traction Study Group

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created an optical coherence tomography (OCT)-based system for the classification of diseases of the vitreomacular interface. The International Vitreomacular Traction Study definition for FTMHs requires detection of FTMHs in at least one OCT scan.[6]

There are two major mechanisms previously described for FTMH formation, anteroposterior vitreous traction and tangential vitreous traction on the foveal retina.[7] The hole usually has an hourglass shape, and the vitreous may or may not be attached to the edge of the macular hole.[6]

The incidence of FTMHs in eyes with AMD is unknown, and the previous literature is limited. The pathogenesis might be tractional from anteroposterior or tangential vitreomacular traction with or without CNV contraction or degenerative which results from a atrophic processes in the underlying choroid and malfunctioning RPE.[8–10] Anti–vascular endothelial growth factor intravitreal injections can also induce vitreoretinal traction leading to the development of a FTMH or anti–vascular endothelial growth factor itself can modulate the activity of CNV and induce contraction of the membrane which may result in FTMHs.[11–13] For FTMHs in the presence of AMD, success rates for anatomical closure after pars plana vitrectomy range between 75% and 89%[11,14,15] and considered significantly lower in comparison with idiopathic FTMHs with anatomical success rates of above 90%.[16]

Because of the lack of normal anatomy and additional findings on clinical and OCT examinations, it can be challenging to differentiate between tractional and degenerative FTMHs in the presence of AMD. We did not find any previous studies that differentiate clinical presentation or surgical outcomes of degenerative FTMHs from tractional FTMHs in AMD patients. The clinical implications of this observation might be significant to patients prognosis.

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The purpose of this study is to describe OCT characteristics of FTMHs in AMD patients.

METHODS

A retrospective, multicenter, observational study of consecutive patients diagnosed with AMD and FTMHs seen by retina specialists between January 1, 2009, and January 3, 2020, at the ophthalmology departments of Meir Medical Center, Kfar Saba, Tel Aviv Sourasky Medical Center, Tel Aviv, Rabin Medical Center, Petach Tikva, Hadassah, Hebrew University Medical Center Jerusalem, Hillel Yaffe Medical Center, and Hadera and Shaare Zedek Medical Center, Jerusalem. The study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board (IRB) of all the above-mentioned medical centers.

Cases were identified by electronic medical records of each department. The inclusion criteria were the presence of intermediate or advanced AMD (geographic atrophy or NV-AMD) which were made according to the severity scale for AMD, AREDS report.[17] The presence of FTMHs, defined as anatomic opening of all the layers of the fovea featuring interruption of all neural retinal layers from the ILM to the RPE.[3] AMD staging was made by a retina specialist with the use of clinical examination, color images, and OCT scans. Exclusion criteria were high myopia, history of retinal detachment, central serous chorioretinopathy, diabetic retinopathy, macular telangiectasias, tractional and degenerative lamellar macular holes, central or branch retinal vein occlusion, central or branch retinal artery occlusion, advanced glaucoma, or optic neuropathy of any kind, visually significant cataract, endophthalmitis, retinal dystrophies, inability to perform OCT or any cause for nonreadable OCT, and any previous intraocular surgery besides uncomplicated cataract surgery.

Data collected included demographics, best-corrected visual acuity, slit-lamp examination, and macular spectral-domain optical coherence tomography.

The best-corrected visual acuity was recorded and reported in Snellen fraction, which was converted into logarithm of the minimal angle of resolution (logMAR) values for statistical analysis.

Optical Coherence Tomography Processing

All OCT images were carefully reviewed and analyzed by two masked retina specialists (G.R and O.S) to ensure a uniform grading analysis. Spectral-domain OCT (Spectralis OCT; Heidelberg engineering, Heidelberg, Germany) was used. OCT parameters

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included external (basal) and internal diameters and interna–lexternal diameter ratio of the FTMHs. External hole diameter, previously described by Yun et al, was defined as the hole diameter at the level of the RPE,[18] and inner hole diameter was defined as the diameter at the level of the ILM previously described by Haouchine et al, [19] as seen in Figure 1. Diameters were measured on OCT scans using the caliper function of each OCT viewer program. The presence of operculum in the posterior vitreous overlying the macula, complete RPE and outer retinal atrophy (cRORA),[20]pigment epithelium detachment (PED), outer retinal tubulation, subretinal hyperreflective material (SHRM) with high reflectivity,[21] hyperreflective foci, central macular thickness (CMT), previously described by Adhi et al,[22] vitreomacular adhesion, posterior vitreous detachment, and epiretinal membrane (ERM) were recorded.

Statistical Analysis

All data collected in the study were inserted into an electronic database by Microsoft Excel 2013 (Microsoft Corporation). Statistical analyses were performed using Minitab Software, version 17 (Minitab Inc, State College, PA). Results are expressed as mean ± SD, median (range) or N (%). For the comparison of continuous and categorical data at the final visit versus baseline the paired *t*-test and McNemar's test were used, respectively. For the comparison of continuous and categorical data between nonpaired groups the Student-*t* and chi–square test were used, respectively. Multivariate binary logistic regression analysis was performed to determine parameters predicting two or more lines of improvement after surgery. For this purpose, we introduced as independent variables those variables that reached a significant level of less than 0.15 in univariate analysis. Based on the binary logistic regression, the area under the receiver operating characteristic curve (AUC) was determined to evaluate the discriminatory ability according to the assessed parameters. The point with the larger Youden index, equal to sensitivity + specificity -1, was defined as the optimal cutoff point. A P value of less than 0.05 was considered statistically significant.

RESULTS

We reviewed the charts of all patients diagnosed with advanced or intermediate AMD in the abovementioned retina clinics, of which 86 eyes of 85 patients diagnosed with FTMH, met the inclusion criteria and enrolled into the study. Forty-nine (57.6%) were women, mean age was 80.31 ± 8.06, (range 57.6–99.0) and mean visual acuity was 1.17 ± 0.58 logMAR (range 0.10–2.00 logMAR).

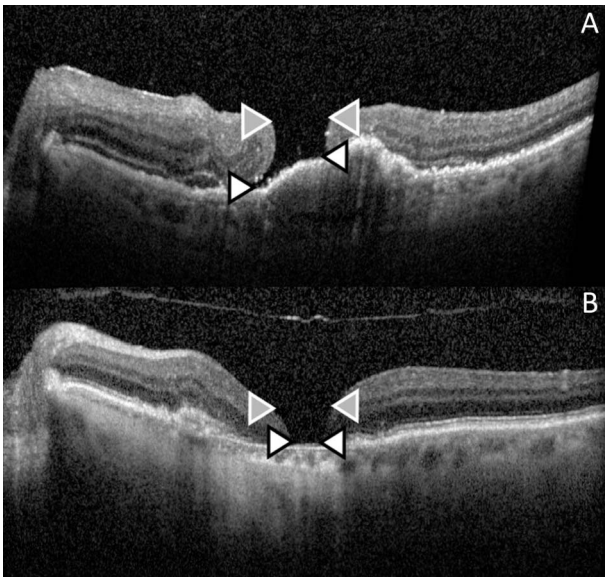

Fig. 1. Optical coherence tomography measurements of tractional and degenerative FTMHs. **A.** Tractional FTMHs, the widest inner diameter (gray arrows) is the maximum distance between the edges of the hole at the level of the ILM. The external diameter (white arrows) is the maximum diameter at the level of the RPE. **B.** Degenerative FTMHs, the widest inner diameter (gray arrows) is the distance between the edges of the hole at the level of the ILM. The external diameter (white arrows) is the maximum diameter at the level of the RPE.

Analysis of OCT images suggested two distinct subtypes of FTMHs defined by specific morphologic features (Figure 2). A total of 50 (58%) FTMH had "inverted trapezoid" (Figure 2, top) appearance with distinctive characteristics of CMT $<$ 240 μm, cRORA, and internal–external ratio $>$ 1.5. We termed this condition "degenerative FTMHs". The second type observed (Figure 2, bottom) was diagnosed in 36 (42%) eyes and had "hourglass" appearance. Its features included CMT $>$ 320 μm, internal–external ratio $<$ 1.5 in contrast with degenerative FTMHs, and the presence of PED or ERM. We termed this subtype "tractional FTMHs."

There were no statistically significant differences in terms of demographics between the groups: For the degenerative FTMHs, the mean age of was 79.4 ± 7.8 years, 29 of them were women (58%), and the visual acuity was 1.15 ± 0.58 logMAR, in comparison with 81.7 ± 8.3 years, 20 (57.1%) women, and visual acuity of 1.20 ± 0.59 logMAR for the tractional hole group (P = 0.21, 0.94, 0.69, respectively).

A total of 58 (67%) eyes presented with NV-AMD, 15 (18%) eyes with geographic atrophy, and 13 (15%) eyes with intermediate AMD. In the degenerative FTMH group, 38 (76%) eyes presented with NV-AMD, and 12 (24%) eyes presented with geographic

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atrophy, and in the tractional FTMH group, 20 (56%) eyes presented with NV-AMD, 3 (8%) eyes with geographic atrophy, and 13 (36%) eyes with intermediate AMD."

Optical Coherence Tomography Findings

Degenerative FTMHs presented with 0% hourglass shape, 100% inverted trapezoid shape, 66% of them had CMT < 240 μm, 14% of CMT > 320, 70% of cRORA, and 70% presented with SHRM with high reflectivity in comparison with 100% hourglass shape, 0% of inverted trapezoid shape, 41% of CMT < 240 μm, 42.9% of CMT > 320, 20% of cRORA, and 25.7% presented with SHRM with high reflectivity in the tractional FTMH group (P = <0.001, <0.001, 0.002, 0.003, <0.001, <0.001, respectively).

External diameter was 393 ± 185 μm, internal diameter was 1,148 ± 701 μm, and internal–external ratio was 3.26 ± 1.81 in the degenerative FTMH group in comparison with 778 ± 349 μm, 716 ± 322 μm, and 1.01 ± 0.53 in the tractional FTMH group (P <0.001, <0.001, <0.001, respectively). In addition, ERM presence and PED presence where significantly higher in the tractional FTMH group (P = 0.02, 0.03, respectively).

Other parameters such as outer retinal tubulation, hyper reflective foci, presence of posterior vitreous detachment, vitreomacular adhesion, and operculum above the FTMH were not found to be statistically significant.

Table 1 presents univariate analysis comparison of degenerative FTMHs and tractional FTMHs.

Table 2 presents binary logistic regression analysis comparison of degenerative FTMHs versus tractional FTMHs. In brief, the only parameter that was significant in differentiating between degenerative versus tractional FTMHs was the internal–external ratio with an odds ratio of 0.05 for an increase in 1.0 of the internal–external ratio. Using an ideal cut-off point of 1.14, an AUC of 0.94 was achieved with a sensitivity of 77.4% and a specificity of 96.0% (Figure 3). With the binary regression model including all of the assessed parameters was applied, an AUC of 0.96 with a sensitivity of 86.2% and a specificity of 91.8% (Figure 4) was achieved. Hourglass shape occurred only in tractional FTMHs, inverted trapezoid shape occurred only in degenerative FTMHs, and outer retinal tubulation occurred only in degenerative FTMHs and were therefore not included in the regression analysis.

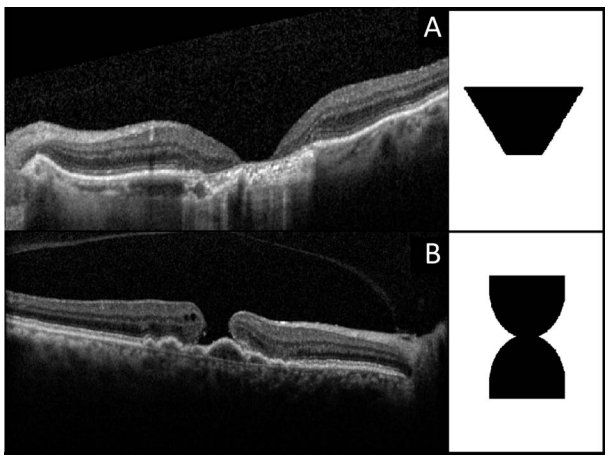

Fig. 2. Morphology of degenerative and tractional FTMH. **A.** Degenerative FTMHs characterized by an inverted trapezoid shape. **B.** Tractional FTMHs characterized by an hourglass shape.

Discussion

Full-thickness macular holes and AMD are two well-known diagnoses, but the presence of both simultaneously is rare and described only in few studies and case reports.[11–15,23–25]

In the past, FTMH diagnosis was clinical and measurements of the FTMHs were not that easy, but in recent years, OCT enables us to observe and analyze additional features of the FTMHs, such as diameter, shape, adherence of posterior hyaloid to the macula, and intra retinal fluid presence.[6] Optical coherence tomography features can also assist in terms of pathogenesis, prognosis, and choice of treatment. The mechanism of FTMH formation in the presence of AMD is not fully understood, and several options were previously postulated including tractional forces from anteroposterior or tangential vitreomacular traction,[6,18] CNV contraction,[7,23] secondary to anti–vascular endothelial growth factor injections,[12,25] and degenerative which results from a atrophic processes in the underlying choroid or malfunctioning retinal RPE.[9,11]

We hypothesize that FTMHs in the presence of AMD may be tractional or degenerative, which may represent different pathologic conditions with different clinical implications. Tractional FTMHs may form by tangential or anteroposterior vitreous traction, ERM, PED, or changes in the CNV membrane.[9,10,25] Although degenerative FTMHs may be caused by atrophic process of the retina secondary to collapsed PED or macular scarring,[8] Cohen et al described retinal pseudocysts in a subset of eyes presenting with geographic atrophy. It was corresponded to optically empty spaces, frequently located in the inner nuclear layer, and they suggested that pseudocysts might correspond to Müller cell degeneration.[26] Retinal pseudocysts might be a part of a degenerative process that eventually leads to the formation of the degenerative FTMHs we observed in this current study.

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Table 1. Univariate Analysis Comparison of Degenerative FTMH and Tractional FTMH

Parameter	Degenerative	Tractional	*P*
Age (years)	79.4 ± 7.8	81.7 ± 8.3	0.21
Right eye	42.0%	57.1%	0.17
Female	58.0%	57.1%	0.94
Visual acuity (logMAR)	1.15 ± 0.58	1.20 ± 0.59	0.69
Hourglass shape	0%	100%	<0.001
Inverted trapezoid shape	100.0%	0.0%	<0.001
CMT < 240 μm	66.0%	41.2%	0.02
CMT > 320 μm	14.0%	42.9%	0.003
SHRM with high reflectivity	70.0%	25.7%	<0.001
Operculum above hole	4.0%	14.3%	0.09
Complete RPE and outer retinal atrophy (cRORA)	70.0%	20.0%	<0.001
External diameter (μm)	393±185	778±349	<0.001
Internal diameter (μm)	1,148±701	716±322	<0.001
Internal–external ratio	3.26±1.81	1.01±0.53	<0.001
PED	22.0%	45.7%	0.02
VMA	14.3%	25.0%	0.35
Partial PVD	10.0%	16.7%	0.55
Complete PVD	83.3%	58.3%	0.09
ERM	30.6%	60.0%	0.03
Hyperreflective foci	40.4%	41.2%	0.95
ORT	22.2%	0.0%	0.09

ORT, outer retinal tubulation; PVD, posterior vitreous detachment; VMA, vitreomacular adhesion.

Both groups presented with similar baseline characteristics including age, gender, and visual acuity, and it might be challenging to differentiate between both types of FTMHs. Thus, the purpose of this study was to assist clinicians in the differentiation process between two types.

Some of the degenerative FTMHs have features complying with atrophy, previously described by Sadda et al.[20] Although, tractional FTMH features resemble to idiopathic FTMHs.[6] But, there is also a possibility of combined pathophysiology. We hypothesize that FTMHs may start as tractional above PED. With time, the PED collapsed, cRORA was formed, and degenerative FTMHs remained. Kabanarou et al, described similar pathology in their small case series of four patients. They showed formation of tractional FTMHs on top of a macular scar or PED; during the follow-up, PED collapsed but the FTMHs remained.[24] In this current study, we found that advanced AMD (NV-AMD or geographic atrophy) presented in all eyes with degenerative FTMHs in comparison with 64% of eyes with tractional FTMHs. In addition, intermediate AMD presented only in eyes with tractional FTMHs but never in eyes with degenerative FTMHs. This observation may potentially influence visual acuity prognosis and treatment.

Today's common practice to treat idiopathic FTMHs is pars plana vitrectomy (PPV) with or without ILM peeling, filling the eye with long-acting gas tamponade (such as SF6 or C3F8) with or without face-down positioning of the patient.[27] There are only few studies that examine FTMH treatment in AMD patients, and there are no any specific guidelines for AMD patients with FTMHs. In this current study, the FTMH size considered large[6] for almost all patients, with external diameter of 393 ± 185 μm and internal diameter of 1,148 ± 701 μm for the degenerative FTMH group and 778 ± 349 μm and 716 ± 322

Table 2. Binary Logistic Regression Analysis Comparison of Degenerative FTMHs Versus Tractional FTMHs

Parameter	R2	Odds Ratio	*P*	Cut-off	AUC	Sensitivity	Specificity
Internal–external ratio	53.20%	0.05 (0.01–0.41)	0.006	1.14	0.94	77.4%	96.0%
Complete RPE and outer retinal atrophy (cRORA)	4.26%	0.18 (0.03–1.22)	0.08	NA	0.75	80.0%	70.0%
PED	3.02%	5.04 (0.62–41.20)	0.13	NA	0.62	45.7%	78.0%
Foveal SHRM with high reflectivity	0.62%	1.48 (0.19–11.36)	0.70	NA	0.72	74.3%	70.0%
CMT < 240 μm	0.15%	1.19 (0.20–7.03)	0.84	NA	0.62	58.8%	66.0%
Binary regression model	61.60%	—	—	>0.49	0.96	86.2%	91.8%

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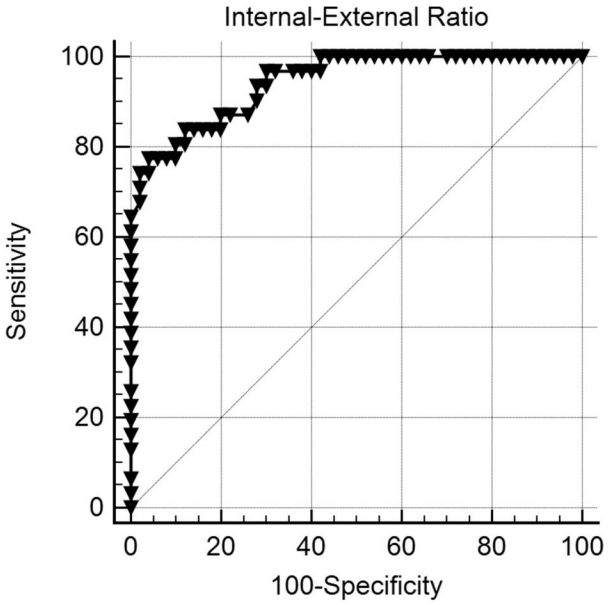

Fig. 3. Receiver-operating characteristic curve with the internal–external ratio as the sole predictor differentiating between a degenerative and tractional FTMHs. A cut-off of 1.14 achieved an AUC of 0.94 with a sensitivity of 77.4% and specificity of 96.0%.

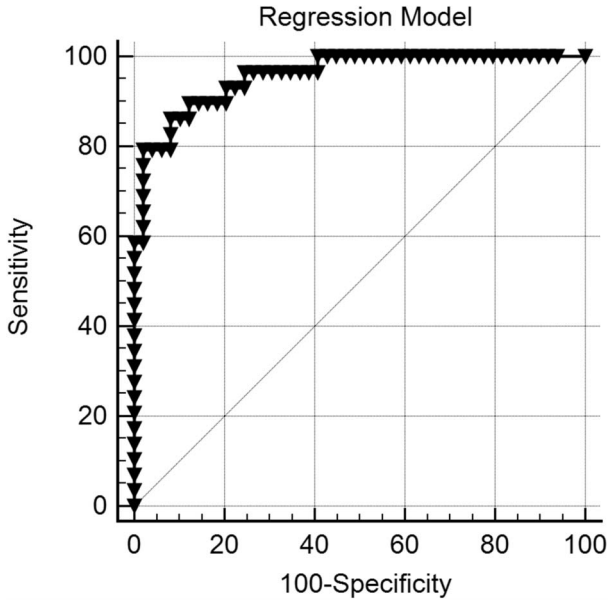

Fig. 4. Receiver-operating characteristic curve with the regression model as the predictor differentiating between a degenerative and tractional FTMHs. An AUC of 0.96 with a sensitivity of 86.2% and specificity of 91.8% was achieved.

μm, respectively, in the tractional FTMH group. Large FTMHs have less favorable surgical success rates in comparison with small–medium FTMHs,[27,28] even with the use of various techniques such as macular hole hydrodissection[29] or inverted ILM flaps.[30] When there is a combination of large FTMHs in the presence of intermediate or advanced AMD, surgical success rates might be even lower. Berinstein et al reported 34 eyes with intermediate AMD and FTMHs that underwent PPV. They reported average FTMH size of 388 μm and 74% anatomical success rate after first surgery.[14] Rao et al reviewed 158 eyes with AMD and FTMHs. Of which, 127 underwent PPV; Six percent of the eyes had GA, which means possible degenerative FTMHs. They discussed that the patient with GA would not be a good surgical candidate. But, they did not differentiate between tractional and degenerative FTMHs.[15] Michalewska and Nawrocki recently published a retrospective case series of 18 eyes with non-NV AMD and large (492–1,073 μm) FTMHs, that underwent PPV with the inverted ILM flap technique. They had an anatomical success rate of 89% for first surgery.[11] We presume that in eyes with AMD one of the reasons for the relatively low success rate, even for small holes, is due to operated degenerative FTMHs.

For degenerative FTMHs, we believe that surgical intervention might not improve the visual acuity, because there are foveal outer retinal layers and RPE atrophy, with poor foveal vision potential. It might be recommended to continue AMD follow-up and treatment, including anti–vascular endothelial growth factor injections, when needed, and do not perform PPV, similar to Rao et al[15] assumption.

This study had several limitations, first of which is its retrospective design. Second, we described and compared tractional and degenerative FTMH characteristics, but we did not follow-up the patients including change in the visual acuity and surgical outcomes for the patients who underwent PPV. Future, larger, prospective studies are needed to better understand the pathophysiology and stages of both tractional and degenerative FTMHs.

CONCLUSIONS

Degenerative and tractional FTMHs may be two distinct clinical entities. This observation may present with diagnostic and therapeutic dilemmas. Discerning degenerative from tractional FTMHs is possible by using OCT features including shape of the FTMH, CMT, internal–external ratio of FTMHs, presence of cRORA, PED, and ERM.

Key words: full-thickness macular hole, traction, degenerative, AMD, OCT.

References

1. Jonas JB, Cheung CMG, Panda-Jonas S. Updates on the epidemiology of age-related macular degeneration. Asia-pacific J Ophthalmol 2017;6:493–497.

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2. Lim LS, Mitchell P, Seddon JM, et al. Age-related macular degeneration. Lancet 2012;379:1728–1738.
3. Ezra E. Idiopathic full thickness macular hole: natural history and pathogenesis. Br J Ophthalmol 2001;85:102–108.
4. Ho AC, Guyer DR, Fine SL. Macular hole. Surv Ophthalmol 1998;42:393–416.
5. Klein R, Klein BEK, Wang Q, et al. The epidemiology of epiretinal membranes. In: Transactions of the American Ophthalmological Society. Vol 92: American Ophthalmological Society; 1994:403–430.
6. Duker JS, Kaiser PK, Binder S, et al. The international vitreomacular traction study group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology 2013; 120:2611–2619.
7. Takezawa M, Toyoda F, Kambara C, et al. Clarifying the mechanism of idiopathic macular hole development in fellow eyes using spectral-domain optical coherence tomography. Clin Ophthalmol 2011;5:101–108.
8. Rishi P, Kasinathan N, Sahu C. Foveal atrophy and macular hole formation following intravitreal ranibizumab with/without photodynamic therapy for choroidal neovascularization secondary to age-related macular degeneration. Clin Ophthalmol 2011;5:167–170.
9. Tabandeh H, Smiddy WE, Sullivan PM, et al. Characteristics and outcomes of choroidal neovascularization occurring after macular hole surgery. Retina 2004;24:714–720.
10. Nowosielska A. Macular hole surgery in the case of wet age-related macular degeneration treated with intravitreal aflibercept. Case Rep Ophthalmol 2019;10:369–373.
11. Michalewska Z, Nawrocki J. Vitrectomy with the inverted internal limiting membrane flap technique in eyes with full-thickness macular hole and dry age-related macular degeneration. Eur J Ophthalmol 2020. doi: 10.1177/1120672120921376. Epub ahead of print.
12. Moisseiev E, Goldstein M, Loewenstein A, et al. Macular hole following intravitreal bevacizumab injection in choroidal neovascularization caused by age-related macular degeneration. Case Rep Ophthalmol 2010;1:36–41.
13. Clemens CR, Holz FG, Meyer CH. Macular hole formation in the presence of a pigment epithelial detachment after three consecutive intravitreal antivascular endothelial growth factor injections. J Ocul Pharmacol Ther 2010;26:297–299.
14. Berinstein DM, Hassan TS, Williams GA, et al. Surgical repair of full-thickness idiopathic macular holes associated with significant macular drusen. Ophthalmology 2000;107:2233–2239.
15. Rao P, Yonekawa Y, Abbey AM, et al. Prevalence and surgical outcomes of macular hole in eyes with age-related macular degeneration. Ophthalmol Retin 2017;1:158–164.
16. Zhao P, Wang S, Liu N, et al. A Review of surgical outcomes and advances for macular holes. J Ophthalmol 2018;2018. doi: 10.1155/2018/7389412.
17. Ferris FL, Davis MD, Clemons TE, et al. A simplified severity scale for age-related macular degeneration: AREDS report no. 18. Arch Ophthalmol 2005;123:1570–1574.
18. Yun C, Oh J, Hwang SY, et al. Morphologic characteristics of chronic macular hole on optical coherence tomography. Retina 2012;32:2077–2084.
19. Haouchine B, Massin P, Tadayoni R, et al. Diagnosis of macular pseudoholes and lamellar macular holes by optical coherence tomography. Am J Ophthalmol 2004;138: 732–739.
20. Sadda SR, Guymer R, Holz FG, et al. Consensus definition for atrophy associated with age-related macular degeneration on OCT: classification of atrophy report 3. Ophthalmology 2018; 125:537–548.
21. Pokroy R, Mimouni M, Barayev E, et al. Prognostic value of subretinal hyperreflective material in neovascular age-related macular degeneration treated with bevacizumab. Retina 2018; 38:1485–1491.
22. Adhi M, Duker JS. Optical coherence tomography-current and future applications. Curr Opin Ophthalmol. 2013;24: 213–221.
23. Okamoto T, Shinoda H, Kurihara T, et al. Intraoperative and fluorescein angiographic findings of a secondary macular hole associated with age-related macular degeneration treated by pars plana vitrectomy. BMC Ophthalmol 2014; 14:1–4.
24. Kabanarou SA, Xirou T, Mangouritsas G, et al. Full-thickness macular hole formation following anti-vegf injections for neovascular age-related macular degeneration. Clin Interv Aging 2017;12:911–915.
25. Querques G, Souied EH, Soubrane G. Macular hole following intravitreal ranibizumab injection for choroidal neovascular membrane caused by age-related macular degeneration. Acta Ophthalmol 2009;87:235–237.
26. Cohen SY, Dubois L, Nghiem-Buffet S, et al. Retinal pseudocysts in age-related geographic atrophy. Am J Ophthalmol 2010;150:211–217.e1.
27. Parravano M, Giansanti F, Eandi CM, et al. Vitrectomy for idiopathic macular hole. Cochrane Database Syst Rev 2015; 2015. doi: 10.1002/14651858.CD009080.pub2.
28. Chng SW, Patton N, Ahmed M, et al. The manchester large macular hole study: is it time to reclassify large macular holes? Am J Ophthalmol 2018;195:36–42.
29. Felfeli T, Mandelcorn ED. Macular hole hydrodissection: surgical technique for the treatment of persistent, chronic, and large macular holes. Retina 2019;39:743–752.
30. Michalewska Z, Michalewski J, Dulczewska-Cichecka K, et al. Temporal inverted internal limiting membrane flap technique versus classic inverted internal limiting membrane flap technique. Retina 2015;35:1844–1850.

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