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Tomographic prognostic indices for large idiopathic macular hole closure: a prospective study

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Keywords
Macular hole, Optical Coherence Tomography, Macular hole closure.

Abstract

Purpose. The study aims to determine the prognostic value of spectral domain Optical Coherence Tomography (SD-OCT) in anatomical closure of large idiopathic macular hole (IMH) after surgery.
Methods. The study included 40 patients with large IMH who underwent MH surgery between January and September 2020. The inclusion criteria required patients to have a minimum of 9 months follow-up after primary MH repair surgery for a large IMH. Patients with secondary MHs or additional ocular diseases that could impact visual acuity, as well as patients with low-quality OCT images, were excluded. The patients underwent a comprehensive eye examination, color fundus photography, and OCT at baseline, 3 months, 6 months, and 9 months after surgery. The SD-OCT parameters measured included minimum diameter, base diameter, macular hole height, hole form factor (HFF), macular hole index (MHI), diameter hole index (DHI), tractional hole index (THI), macular hole angle, and macular hole area index (MAI).
Results. Univariate and multivariate regression analyses demonstrated that minimum diameter, THI, and MAI were significantly correlated with anatomical success, with THI being the most important index in predicting hole closure.
Conclusion. These findings suggest that SD-OCT parameters can be useful predictors of the outcome of MH repair surgery. Further studies are recquired to study these indices.

Introduction

The idiopathic macular hole (IMH) is a rare condition that causes a complete interruption of all retinal layers at the foveola, leading to a profound impairment of central vision. The pathophysiology involves tangential and anteroposterior traction due to incomplete posterior vitreous detachment [1]. Optical coherence tomography (OCT) is the gold standard for diagnosing and managing IMH, providing measurement of diameter and vitreoretinal interface analysis to guide surgical intervention. Additionally, recent research has emphasized the prognostic value of OCT by measuring several tomographic indices. Patients with large macular holes have poorer surgical outcomes, but various techniques, such as inverted internal limiting membrane (ILM) flap techniques, have been proposed to improve success rates [2]. The aim of this study was to evaluate correlation of various spectral domain optical coherence tomography (SD-OCT) parameters with anatomical outcomes after large IMH repair surgery with inverted ILM flap technique.

Methods

A prospective descriptive study was conducted, which included 40 patients diagnosed with large IMH who underwent MH surgery between January and September 2020. Inclusion criteria consisted of patients who underwent primary MH repair surgery for a large IMH and had a minimum of 9 months follow-up. Exclusion criteria included subjects with secondary MHs or additional ocular diseases that could impact visual acuity, well as patients with low-quality OCT images. All patients underwent a comprehensive eye examination, including best-corrected visual acuity (BCVA) testing (The BCVA was assessed using Snellen's chart and was converted to logarithm of the minimum angle of resolution (logMAR) for statistical analysis), dilated fundus examination with slit-lamp biomicroscopy, color fundus photography, and OCT at baseline, 3 months, 6 months, and 9 months after surgery.

Spectral Domain OCT

OCT images were obtained using the Spectral Domain Spectralis™ OCT (Heidelberg Engineering®, Heidelberg, Germany) after pupil dilation with 0.5% Tropicamide and 10% Phenylephrine drops. A dense mode scan of the macular cube was performed with B scans passing through the entire surface of the MH. The scan with the maximum MH diameter was analysed to measure diameters and tomographic indices.
The data extracted from the SD-OCT scans included the presence of epiretinal membrane (ERM), cystic edges at the macular hole, and retinal pigment epithelium (RPE) proliferations. ERM was defined as the first hyper-reflective line internal to the ILM if present. Cystic edges were identified if intraretinal cystoid spaces were present at the edges, and preoperative RPE proliferations corresponded to hyperreflective protrusions above the RPE line in the macular hole.

Measurements

The preoperative OCT images was exported as a 1008 × 596 pixel resolution JPEG (Joint Photographic Experts Group) file to ImageJ (Open source software- version 1.52). A scale of 17 pixels per 200 microns was set.
After being selected with the "straight line" tool, the following parameters were measured with the "analysis/measure" function

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- Minimum diameter between edges
- Maximum diameter at base
- Left and right arm's length.
- Macular hole height

From these measurements, the following indices were derived [3,4,5]:
-Hole form factor (HFF) = (right arm length + left arm length)/ maximum base
- Macular hole Index (MHI) = height/maximum diameter
- Diameter hole index (DHI) = minimum diameter/maximum diameter
-Tractional hole index (THI) =height/minimum diameter
- Macular hole angle was defined by the angle between the nasal or temporal arm and the maximum basal diameter. Using the « angle tool » in Image J right and left macular hole were measured. Average of nasal and temporal angle was used for analysis [6].
Macular hole angle = (right macular hole angle + left macular hole angle)/2

Using the polygonal tool, the macular hole area and the total area with includ the area of intraretinal fluid and the macular hole at centre, were calculated **(Figure 1)**.

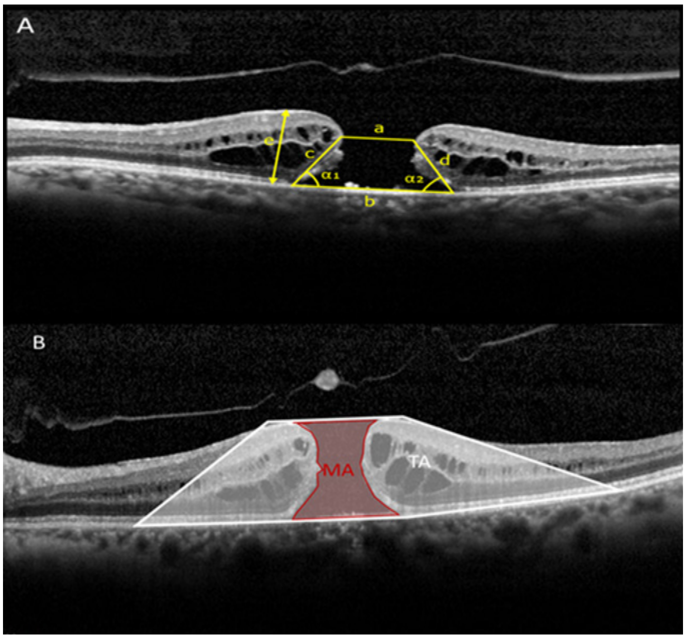

Figure 1. Optical coherence tomography scan measurements. (A) a. minimum diameter; b: maximum diameter; c,d: right and left arm; e: height; α_1,α_2: macular hole angle. (B) MA: macular hole area; TA: total area.

From these measurements, the following indice was derived [3]:
- Macular hole area index (MAI) = macular hole area/ total area
Macular hole surgery:

All patients underwent 23-gauge pars plana vitrectomy with inverted ILM-flap technique using Brilliant Blue Green dye and sulphur hexafluoride (SF6) 20% gas tamponade by the same well-experienced vitreoretinal surgeon between January and September 2020 **(Figure 2).**

Follow up outcomes

All patients underwent a complete eye examination with SD-OCT scans at 1, 3, 6 and 9 months after the surgery.

Anatomical outcomes

Tomographic closure of the MH was defined as the restoration of all or part of the retinal layers above the pigment epithelium in a continuous or discontinuous manner.
We defined failure of closure as the lack of restoration of continuity between the two edges of the MH.
In our study, the patients were divided into two types of anatomical outcomes

- Type1: patients with MH closure.
- Type 2: patients without MH closure.

Statistical analysis

The data collected were analysed using SPSS software version 26. For quantitative variables difference between the 2 groups were analysed using the Mann-Whitney test, while the Chi-square Test was used for qualitative variables. Multivariate analysis was performed using logistic regression analysis.

Results

In this prospective study, 40 patients with large IMH who underwent MH repair surgery were included, resulting in 40 eyes being analysed. The mean age of the study patients was 65.97 ± 4.7 years, with 13 men and 27 women (sex ratio of 1:2). At presentation, all patients complained of diminution of vision, with 27 patients reporting central scotoma and 10 patients reporting metamorphopsia. The mean duration of symptoms was 7 ± 2.5 months, and the mean baseline BCVA was 1.26 ± 0.35 LogMAR. The MH closure rate after surgery was 90% (36 eyes). The mean BCVA at postoperative 9 months was 0.69 ± 0.42 LogMAR. On SD-OCT examination at baseline, ERM was present in 3 eyes, and cystic edges were present in 36 eyes. RPE proliferations on SD-OCT were present in 35 eyes . The mean minimum diameter was 655.48 ± 167.16 µ, the mean base diameter was 1290.15 ± 369.21 µ, the mean macular hole height was 1218.43 ± 309.77 µ, the mean macular hole angle was 65.66° ± 7.3°, the mean total area was 3,481 ± 1,588 mm², and the mean macular area was 1.014 ± 0.415 mm². The derived macular hole indices were as follows: mean HFF was 1.334 ± 0.440, mean MHI was 0.998 ± 0.321, mean THI was 2.033 ± 0.778, mean DHI was 0.517 ± 0.115, and mean MAI was 0.295 ± 0.052.Complete recovery of the external limiting membrane and ellipsoid zone was observed in 83% and 64% of the patients, respectively, 9 months after surgery.
Univariate and multivariate regression analyses were conducted to determine the relationship between the various parameters and hole closure. Only minimum diameter, THI, and MAI were found to be significantly correlated with anatomical success (p=0.032, p=0.013, p=0.042, respectively). The larger the size of the hole, the higher the risk of non-closure, and the higher the MAI value, the higher the risk of closure failure. However, a positive correlation was found between the THI and the anatomical success of the surgery **(Tables I, II, III) (Figure 2).**
Of the three SD-OCT parameters, THI was found to be the most important index in predicting hole closure.

Discussion

The first study to use OCT to analyse MH preoperatively was published by Ip et al in 2002 [7]. Since then, various studies have been published describing the role of analysing quantitative and qualitative parameters predicting the anatomic closure following MH repair surgery.
In our study, we noted a negative correlation between the size of the MH and the closure rate after surgery (p=0.032). In a study involving 258 eyes, Soon Wang et al. [2] considered a threshold value of minimal diameter < 630 µm to predict macular hole closure after vitrectomy and ILM peeling. The authors noted a hole closure rate of 94% for a minimal diameter between 400 µm and 650 µm, and 76% for holes larger than 650 µm. For this reason

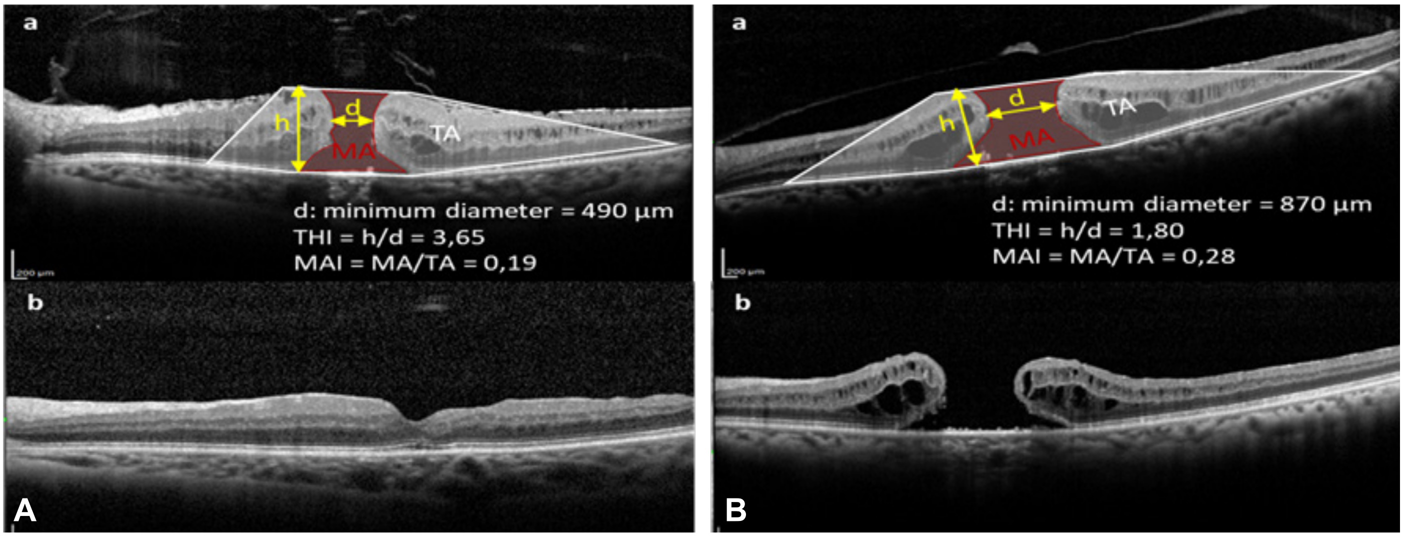

Figure 2. **Minimum diameter, Tractional hole index (THI) and macular hole area index (MAI) in two different cases of macular hole.**
(A) (a) preoperative SD-OCT image of a 69-year-old patient showing an idiopathic full-thickness macular hole with minimum diameter = 490 µm, THI=3.65 and MAI=0.19. (b) an SD-OCT image obtained 9 months after surgery showing anatomical closure of the macular hole.
(B) (a) preoperative SD-OCT image of a 65-year-old patient showing an idiopathic full-thickness macular hole with minimum diameter = 870 µm, THI=1.80 and MAI=0.28. (b) an SD-OCT image obtained 9 months after surgery showing unfavourable anatomical outcome.

Table I. **Correlation between macular hole parameters and anatomical outcomes (group 1 with macular hole closure and the group 2 with macular hole non-closure).**

Germes	Nombre d'yeux	Pourcentage (%)	p
MD (µm)	602	756	0,210
BD (µm)	1285	1306	0.783
Height (µm)	1224	1202	0,951
THI	2,05	2	0,406
DHI	0,51	0,54	0,508
MHI	1,01	0,96	0,580
HFF	1,38	1,2	0,424
MA (mm²)	1,018	1,002	0,783
TA (mm²)	3,562	3,200	0,432
MAI	0,29	0,3	0,794
MH angle (°)	65,73	65,45	0,667

MD: minimum diameter; BD: base diameter; HFF: Hole Form Factor; THI: Tractional Hole Index; DHI: Diameter Hole Index; MHI: Macular Hole Index; MAI: Macular Hole Area Index; MH: Macular Hole; p: Degree of significance.

they have determined that a size of 650 µm was a more appropriate threshold for categorizing MHs as either medium or large. Their study demonstrated that conventional surgery for large macular holes (>650 µm) was less effective and recommended techniques such as inverted flap. Their findings indicated that calculating derived indices for MH measurement from basic ophthalmic measurements did not provide a significant advantage in predicting anatomic closure and functional success after MH surgery. Instead, they identified the preoperative base diameter as the most critical factor in predicting both anatomic and functional success. Unlike our study, the basal diameter did not have any influence on the anatomical outcome of the surgery. In our series, we did not find a statistically significant correlation between the height of the MH and the anatomical outcome, which is consistent with most studies [8,9,10,11]. However, in a series of 38 patients who underwent MH surgery, Haritoglou et al. studied the association between certain tomographic parameters and long-term functional outcome. They found a negative correlation between height and visual acuity at 5 years after surgery [12]. In 2008, Ruiz-Moreno et al. described two additional indices [9]. These indices have a drawback in that they primarily consider only one of the two tractional forces responsible for MH formation. For instance, the DHI is based on the ratio of the minimum diameter of the MH to the base diameter, which indicates the strength of tangential traction at the fovea, assuming that the tractional force is at its maximum when the inner diameter of the MH is equal to the base diameter. A correlation between DHI and anatomical success has been described by some authors [3,6]. In a recent study, Venkatesh et al. [3] noted that a DHI <0.505 is a favorable prognostic factor. However in our study w did not notice any correlation between DHI and anatomical closure. Conversely, the THI is based on the ratio of the maximal height of the MH to the minimum diameter, which represents primarily the antero-posterior vitreomacular traction and/or retinal hydration responsible for MH formation and less of tangential traction. The THI was found to be significantly correlated with anatomical and functional outcome [3,6,9,13,14]. In our study, THI had the best predictive value for anatomical success among all tomographic parameters (p=0.013). In addition, a few other indices, such as the HFF and MHI, take into account both the tractional forces involved in MH formation. Ulrich et al. [4] in 2002 have presented a study based on the measurement of the HFF. They have expected that HFF which incorporates the nasal and temporal arms of the hole edges divided by the maximum diameter provide a more comprehensive picture of the MH. However Haritoglou et al. [12] have found a weak correlation between HFF and anatomical outcome. In our study, we did not ot find any correlation between HFF and the rate of closure.

In 2004, Kusuhara et al. [5] introduced the MHI, which employs the ratio of the MH height to the base diameter. By using a ratio rather than linear measurements, they were able to avoid the impact of axial length on transverse measurements. Their study found a significant correlation between the MHI and postoperative macular thickness. However, in our series, no correlation was found between MHI and the anatomical outcome.

Table II. Multivariate regression analysis between spectral-domain optical coherence tomography parameters and macular hole closure.

Tomographic parameters	p	OR	Confidence interval	Moriyama et Hofling-Lima (Brésil), n=366 %
Macular Hole diameter	0,032	1,003	1,003 - 1,057	45.2
Tractional hole index (THI)	0,013	1,056	1,016 – 1,098	21.7
Hole Form Factor (HFF)	0,065	0,027	0,001 - 1,248	39.7
Macular Hole Area	0,132	1,000	1,000 - 1,000	1.67
Macular hole Area Index (MAI)	0,042	0,000	0,000 - 0,072	-

P: degree of significance, OR: odds ratio.

Chhablani et al. [6] have conducted a study to evaluate the utility of measuring the MH angle as a predictor of anatomical closure following MH surgery. Our results were consistent with those in the literature we have found that measuring the MH angle was not useful in predicting anatomical outcome after surgery by the reason that MH angle is a unidimensional measure that gives little information about the tractional forces responsible for MH formation. The edges of macular holes and the retinal surface are curved, making linear measurements potentially inaccurate. Fortunately, with advances in computing technology, it is now possible to automatically measure the area of irregularly shaped structures. Venkatesh et al. [3] have published a study in 2019 that developed three new area indices that are strongly correlated with MH closure. The MAI, in particular, appears to be the most significant predictor of anatomical success after MH surgery.

Table III. Comparison of qualitative tomographic data between the "Macular Hole Closure" group and the "Macular Hole Non-Closure" group.

	Group « MH closure » n=36		Group « MH non closure » n=4		P
	count	Pourcentage (%)	Nombre	Pourcentage (%)	
Intraretinal cystic cavities	32	88%	4	100%	0,168
RPE Proliferations	32	88%	3	75%	0,224
ERM	3	8%	0	0%	0,298

MH: macular hole; RPE: retinal pigment epithelium; ERM: epiretinal membrane; n: number, p: degree of significance.

In our series, we noted a statistically significant correlation between MAI and the anatomical outcome after the intervention. Regarding the qualitative parameters, the study by Chhablani et al. [6] did not demonstrate any correlation between the presence of cystic cavities, ERM, and RPE proliferations with the anatomical outcome, either in the univariate or multivariate analysis. As far as we know, this is the first study in Tunisia that has compared various prognostic factors within the same group of patients. Our study benefited from the fact that all patients with MHs were treated using a consistent surgical technique done by the same well-experienced surgeon, and all measurements were taken simultaneously using the same open-access imaging software. However, the study was limited by a small sample size and a relatively short follow-up period.

Conclusion

In conclusion, OCT remains the gold standard for assessing pathologies of the vitreomacular interface, particularly MHs. The positive diagnosis of MHs and therapeutic indications rely on OCT, which has also provided prognostic information by accurately measuring the size of the hole and studying various prognostic indices, which may influence the choice of surgical techniques and potentially offer new approaches for poor prognostic MHs. Further studies are necessary to continue exploring this direction in the future.

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