"VICTOR BABEŞ" UNIVERSITY OF MEDICINE AND PHARMACY
FROM TIMISOARA

FACULTY OF MEDICINE

DEPARTMENT OF OPHTHALMOLOGY

STELLA IOANA PATONI

PhD THESIS

MACULAR HOLE. CORRELATIONS BETWEEN SIZE, SHAPE, SURGERY AND FINAL AV

– A B S T R A C T –

Scientific leader

PROF. UNIV. DR. MIHNEA MUNTEANU

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I. INTRODUCTION

The doctoral thesis entitled "Macular Hole. Correlations Between Size, Shape, Surgery and Final Visual Acuity" is part of the concerns of the research group of Victor Babes University Timisoara. The thesis was developed within the Central Military Emergency University Hospital "Dr. Carol Davila" Bucharest and contains original contributions in the field of ophthalmology, the department of vitreous-retinal surgery. The work contains 122 pages and opens with an introduction in which I motivated the choice of the topic and its importance, followed by the deepening of the scientific research which is carried out in two significant chapters entitled General Part and Special Part each with sub-chapters that deal with various aspects of the topic addressed and ends with the chapters entitled: Discussions, Conclusions, Own Contributions, Limits of the study.

The thesis is part of the current concerns. It is in line with the current concerns at the international and national level, opening new directions of research in the field of artificial intelligence that leaves its mark elegantly in all fields, including ophthalmology.

Over time, this pathology has concerned the scientific community, but it has received increased attention in recent years as the pathophysiology of the macular hole has been better understood with the help of high-performance imaging techniques.

Our study took place during the COVID-19 pandemic, when society was dominated by change, impacting people's way of life and thinking. Progress supported by an increasingly strong technological base is making its way into the daily lives of people.

As medical practice evolves, understanding the complexities and dynamics of hole formation, shape, and size predicts surgical success.

The main objectives of this research are

• increasing the visual acuity of the macular hole patient for whom surgical treatment is the only chance to improve the quality of life.

• establishing the performance of surgical techniques using OCT imaging as the reference method

• determining the OCT parameters that can predict the success of the operation and the postoperative visual acuity

• evaluating the feasibility of using these parameters to develop a fully automated 3D OCT image analysis of the Deep Learning model for more accurate measurement of macular hole parameters, potentially helping to automate these measurements.

This paper is structured in several main sections, including an exhaustive literature review, a detailed description of the methodology and theoretical frameworks used, a presentation of the results obtained, and a similar discussion of these results in the context of existing knowledge making original contributions related to the correlations between the size and shape of the macular hole.

II. GENERAL PART

The macula is a small area in the retina's center and is the only area of the eye that makes it possible to see clearly and in colors fine details.

The macular hole represents a rupture in the retinal tissue, the macula, a severe action generally occurring in patients older than 60, women being more predisposed than men. This pathology affects only the central vision; the peripheral vision is not being modified.

The first sign that appears among patients is a distorted vision in that straight lines seem bent or curved, and difficulties in reading and recognizing faces. Sometimes, an absolute central scotoma can be observed in the central visual field. This makes everyday activities such as reading or writing impossible.

Most of the time, the appearance of the macular hole is idiopathic. However, certain conditions can increase the risk of forming a macular hole, such as diabetic eye disease, chronic macular edema, myopia. Rarely a strong blunt eye trauma or family antecedents can trigger the appearance of this pathology.

Considering the fact that no other ophthalmologist has delved into this topic, we chose this topic to highlight the correlation between the size of the hole and postoperative visual acuity in order to identify the characteristics and risk factors of Romanian patients, which could influence this pathology and to compare the results obtained with international studies.

The topicality of the theme proposed for the study derives from the constant interest in the last decades for increasing visual acuity through various surgical techniques to reduce the peeling damage of the internal limiting membrane.

The first part of the thesis (chapters 1-5) reviews the literature data regarding the current state of scientific knowledge in this field.

In addition to the known and already cited data in specialized literature, how technology individualizes the architecture of the retina through the imaging progress represented by OCT is mentioned in the general part. OCT provides in vivo images without affecting the tissue, with a very fast scanning speed. The retinal layers can be segmented and analyzed; the macular holes can be measured, being able to adapt the surgical approach accordingly and explain to the patient the chances of recovery and the post-operative gain. This type of examination supports the diagnosis and the post-operative evolution, representing an advantage for the doctor and the patient because the monitoring can be done quickly and efficiently.

The innovative character of the work resides in reiterating once again the value of 2D measurements that can predict surgical success and in the fact that these measurements can be the basis for the implementation of an artificial intelligence system that quickly and precisely identifies the degree of post-operative recovery.

III. THE SPECIAL PART

The second part of the thesis, entitled Special Part, presents the original contributions made by the thesis.

In this part, the research carried out during the doctoral program is described in order to achieve the objectives of the thesis. Before describing the research, the objectives of the research are stated (chapter 1.1), as well as the general methodology of the research (chapter 1.3). Next, three sub-chapters (2.2, 2.3, and 2.4) describe the research carried out to achieve the following goals:

1. General objectives

The primary objective is to increase the quality of life by increasing AV.In order to achieve maximum visual acuity, the surgical technique is individualized for each patient depending on the measurements obtained preoperatively with the help of the OCT.

The secondary objectives are the effectiveness of macular dyes that facilitate the essential surgical stage, namely ILM peeling, monitoring the effectiveness of gas endotamponade, and the need for intervention to cure cataracts after vitrectomy.

The tertiary objectives were the monitoring of IOP changes during the study period, the involvement of the fellow eye, the occurrence of complications, and their management if they existed.

2. Material and methods

The research is based on mixed methodologies, including analyzing additional data from this study, such as post-operative posture maintenance and the impact of systemic pathology, such as diabetes and hypertension.

In order to be enrolled, all subjects gave their consent in writing for the performance of OCT scans and surgery.

It was considered to create a group of 32 patients, meaning 40 eyes, 27 women and 13 men aged between 65-70 years, who were distributed in subgroups subjected to therapeutic intervention, depending on the minimum diameter measured on the preoperative OCT in the following order: <250 μm, <550 μm and >550 μm.

The criteria according to which the patients were selected are the following:

• Inclusion criteria:

1-patients with macular holes newly discovered or being monitored in the clinic

2-patients in whom well-informed consent was obtained before the surgical procedure

3-patients who did not have diseases that contraindicate surgical intervention, patients without specific or non-specific allergic reactions, symptoms of acute infection (fever, general malaise)

4-patients whose underlying diseases (hypertension, heart failure, diabetes) were correctly balanced

5-total macular holes FTMH

6-1 year post-interventional follow-up

• Exclusion criteria:

1-macular holes>1000 microns

2- optic nerve atrophy

3-macular pathologies (wet or dry AMD)

4-retinal pathologies (diabetic retinopathy, artery or vein occlusion, previous laser)

5-lamellar macular holes, traumatic or from high myopia

The thesis is part of the current concerns regarding analysis methods. The data were collected and grouped using Microsoft Excel. As an application for statistical analysis, IBM SPSS Statistics V28 was used.

In order to see the extent to which certain factors influence visual acuity, multiple linear regression was used, and the ROC analysis allowed us to evaluate to what extent certain numerical variables are relevant to distinguish between a good visual acuity, for example, and a less good one.

3. Results

The subjects of this study (13 men – 32% and 27 women – 68%) were aged between 65 and 70 years. The closure of the macular hole was achieved in 92% of cases.

Summarizing better visual acuity at baseline, with a smaller mean diameter, increases postoperative outcomes.

Increasing the time to the doctor's presentation and failure to respect the postoperative face-down position leads to a worse recovery.

From the ROC curve analysis, we deduced that indices such as minimum hole diameter, MHI, THI, and HFF could successfully predict macular hole closure, while DHI did not.

Evaluating the results between the two categories of patients in whom we used lutein-based or artificial dyes, the results are similar without statistical significance.

The difference between the proportions before and after cataract surgery is statistically significant: p-value < 0.001. This is due to the acceleration of pre-existing cataracts after vitrectomy surgery.

During the whole study, the mean intraocular pressure fluctuations were minor, with no differences between intraocular pressure before surgery and after one year, although the p-value = 0.596 is not significant.

We did not register any inflammatory reactions in the anterior chamber during the study, a single case of corneal erosion that resolved until the 1-month follow-up.

The status of the I.S.: O.S. junction, or the ellipsoid zone in OCT, is crucial in predicting the outcome for a patient. Type 1, which has no foveal neurosensory retinal (NSR) defect, has a positive outlook. In contrast, type 2, which has a foveal NSR defect, has room for improvement. Therefore, accurate diagnosis and timely intervention can significantly improve the patient's condition.

4. Discussions

This study introduces a highly reliable and accurate technique for measuring and segmenting macular holes in two-dimensional data, offering an assertive and dependable approach to diagnose and treat this condition.

The use of high-resolution SD-OCT allows for precise 2D imaging of macular hole geometry; however, the laborious measurements required by human observers necessitate the development of new time-saving techniques.

Ip et al. conducted a pioneering study on macular holes (M.H.) in 2002 using OCT before surgery. Their research revealed that M.H. less than 400 μm had a high anatomic closure rate of 92%, while M.H. greater than 400 μm had a lower closure rate of 56%. These findings can help guide treatment decisions and improve outcomes for patients with M.H.

Numerous studies have unequivocally demonstrated the paramount importance of macular hole measurements and the associated indices, such as hole forming factor (HFF), macular hole index (MHI), diameter hole index (DHI), and tractional hole index (THI), in accurately predicting the closure of anatomical defects and visual improvement after M.H. repair surgery.

In 2004, Kusuhara S and their team developed an index called the Macular Hole Index (MHI) that is based on OCT recordings of preoperative macular hole configuration. This index is very helpful in assessing macular holes and can provide valuable insights to healthcare professionals.

A minimum MHI value of 0.5 is a reliable predictor of postoperative visual acuity in patients, as noted by experts.

The study conducted by J.M. Ruiz Moreno and his team in 2008 calculated three indices: MHI, DHI, and THI. The results showed that both MHI and THI have a significant correlation with postoperative BCVA at three months, whereas DHI did not show any significant correlation. Our recent study has confirmed the findings, highlighting that MHI and THI are statistically significant, while DHI does not hold any statistically significant value. These results could be very helpful in developing more targeted treatments for patients with postoperative BCVA concerns.

In 2020, Ramesh Venkatesh et al. studied the correlation between tomographic indices and anatomical success in wide macular hole (M.H.) surgery. The study aimed to identify the most reliable indices to predict surgical success. To achieve this, the researchers performed an extensive analysis of the Receiver Operating Characteristic (ROC) curves for each index, including the HHF, MHI, and THI. The study revealed that the MHI and THI indices indicate type 1 closure, while DHI is associated with type 2 closure. These findings could help guide surgical decisions and improve success rates in wide macular hole surgery.

Puliafito's research has shown a correlation between the HFF value and the anatomical success rate of patients. Patients with an HFF greater than 0.9 have a high success rate of 80%, while those with an HFF under 0.5 have a lower success rate of less than 25%. In our own research, we were able to achieve a 92% success rate using the technique that we employed despite the varying HFF values ranging from 0.809 to 1.009.

These findings are valuable and can be used to optimize treatment plans and improve patient outcomes.

According to M Roth and his team, the minimum linear diameter (MLD) is a much stronger indicator of postoperative visual acuity than the basal diameter. It is interesting to note that Steel et al. have suggested a threshold of approximately 500µm for MLD, but we have set a higher threshold of 550µm. These findings can be used constructively in future research to explore the relationship between MLD and postoperative visual acuity in greater detail.

During a medical procedure, the physicians were faced with a decision on the most effective method to endotamponade for patients who would find it challenging to maintain a face-down position for over seven days due to systemic complications. Based on a study conducted by Yu Y.P. in China, it has been established that using gas instead of sterile air is a more effective option for treating macular holes with a diameter of 650 µm or more. This valuable information can help doctors make informed decisions and provide better patient care.

According to two randomized controlled trials (RCTs), it has been confirmed that face-down posturing is not required for small macular holes (<400 µm). However, in our practice, we advise our patients to sit face down for one week, regardless of the size of their macular hole, to ensure a full and speedy recovery.

The future of our studies will involve gathering a multitude of data samples and developing advanced algorithms for automated segmentation, 3D reconstruction, and measurement. These exciting new tools have the potential to transform our experiments, making them more precise and significantly reducing any errors that could result from manual processes.

5 .Conclusions

Our study is the first study conducted in Romania on the topic of macular holes. It shows a 92% increase in postoperative visual acuity and makes a scientific contribution supporting the hypothesis that surgery is the only option for improving visual acuity.

The repeatability and reproducibility of the manual measurements performed in our study on SD-OCT have also been shown to be good in previous studies.

This is a preliminary study to develop a fully automated Deep Learning model 3D OCT image analysis for more accurate measurement of macular hole parameters, potentially helping to automate these measurements.