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GENERAL DESCRIPTION OF WORK

Relevance of the topic. Diabetic retinopathy (DR) is the leading cause of blindness among working age population in developed countries[1,2,3,4]. Estimates show the presence of moderate to severe DR, significantly worsening the quality of life and working ability in 3-5% of the world's diabetic population[5]. According to the State Statistics Committee of the Republic of Azerbaijan, 287,466 patients with diabetes mellitus were registered in medical institutions in 2020 (2.9% prevalence among the population) (source: www.stat.gov.az). In accordance with the Decree of the President of the Republic of Azerbaijan, dated February 12, 2004 on the application of the Law of the Republic of Azerbaijan "On state care for persons suffering from diabetes mellitus" and the Decree of the Cabinet of Ministers of the Republic of Azerbaijan dated November 26, 2010, improving the quality of life of patients with diabetes mellitus and reducing disability related to diabetes has been identified as a priority.

No prospective randomized trial that has investigated the results of surgical treatment of diabetic retinopathy that meet the requirements of evidence-based medicine, was conducted after Diabetic Retinopathy Vitrectomy Study (DRVS, 1990)[6,7]. However,

[1] Klein, B.E. Overview of epidemiologic studies of diabetic retinopathy // Ophthalmic Epidemiol, – 2007; – vol.14(4): – p.179–183.

[2] Moss, S.E., Klein B.E. The 14-year incidence of visual loss in diabetic population // Ophthalmology, – 1998; – vol.105, – p.998-1003.

[3] Рустамова, Н.М. Сравнительная оценка возраста лиц, впервые признанных инвалидами по различным заболеваниям глаз // Офтальмология, – 2012; – vol.9(1): – p.80-82.

[4] Qasımov, E.M., Rüstəmova N.M. Oftalmologiyada əlilliyin birincili və ikincili profilaktikasının əsas istiqamətləri / Akademik Zərifə Əliyevanın 90 illik yubileyinə həsr olunmuş beynəlxalq elmi konfransın materialları toplusu, Bakı, – 2013, – s.56-57.

[5] Resnikoff, S. Global data on visual impairment in the year 2002/ S. Resnikoff, D. Pascolini, D. Etya'ale [et al.] // Bull World Health Organ, – 2004 Nov; – vol.82(11): – p.844-51.

[6] Diabetic Retinopathy Vitrectomy Study Research Group. Early vitrectomy for severe proliferative diabetic retinopathy in eyes with useful vision. Clinical application of results of a randomized trial. Diabetic Retinopathy Vitrectomy Study Report 4 // Ophthalmology, – 1988; – vol.95: – p.1321–1334.

over the period since the DRVS study, significant advances have been made in improving surgical techniques and instrument technology, as well in studying the pathogenesis of diabetic retinopathy. These advances include primarily the use of intraoperative endolaser photocoagulation, wide-angle imaging systems, perfluorocarbon fluids, intraoperative dyes, and intravitreal injections (anti-VEGF, steroids). The advances have helped to improve the safety of operations, reduce the surgical risks, and expand the indications for vitrectomy in diabetic retinopathy. The optical coherence tomography (OCT), which has appeared in recent years, has made it possible to study the anatomy of the macula *in vivo*. OCT technology allowed to study in detail the various changes in the vitreomacular interface in diabetic retinopathy and to expand the indications for vitrectomy for different types of vitreomacular traction. At the same time, reports on the effficacy of removing the internal limiting membrane during vitrectomy for vitreomacular traction are contradictory[8,9]; there are also no data on the results of removing the inner limiting membrane in other complications of DR.

E. de Juan and D. Hickingbotham first proposed a mini-invasive 25-gauge vitrectomy technique in 1990[10], however, since the existing technologies were not compatible with it, the technique did not enter the clinical practice until 2002 (when G. Fujii reintroduced it again[11]). In 2004, C. Eckardt proved the safety and

[7] Diabetic Retinopathy Vitrectomy Study Research Group. Early vitrectomy for severe vitreous hemorrhage in diabetic retinopathy. Four-year results of randomized trial. Diabetic Retinopathy Vitrectomy Study report 5. // Arch Ophthalmol, – 1990; – vol.108: – p.958–964.

[8] Yamada, Y. Systemic factors influence the prognosis of diabetic macular edema after pars plana vitrectomy with internal limiting membrane peeling Y. Yamada, K. Suzuma, M. Ryu [et al.] // Curr Eye Res, – 2013; – vol.38(12): – p.1261-1265.

[9] Romano, M.R. Macular hypotrophy after internal limiting membrane removal for diabetic macular edema / M.R. Romano, V. Romano, J.L. Vallejo-Garcia [et al.] // Retina, – 2014; – vol.34(6): – p.1182-1189.

[10] de Juan, Jr E., Hickingbotham D. Refinements in microinstrumentation for vitreous surgery // Am J Ophthalmol, – 1990; vol.109: – p.218–220.

[11] Fujii, G.Y. A new 25-gauge instrument system for transconjunctival sutureless vitrectomy surgery / G.Y. Fujii, E. de Juan, M.S. Humayun [et al.] // Ophthalmology, – 2002; vol.109: – p.1807-1813.

effectiveness of an integrated 23-gauge vitrectomy system[12], and in 2009, Y. Oshima proposed a 27-gauge vitrectomy[1313]. The aim of reducing the diameter of the instruments is to reduce the surgical trauma and shorten both the duration of the surgery and the postoperative rehabilitation of patients. The disadvantages of mini-invasive vitrectomy are reduced aspiration rate, fragility of surgical instruments, and difficulty in performing complex maneuvers. At the same time, the injection and removal of silicone oil through small incisions takes longer, and the light probes used in mini-invasive surgery provide less light (50% or less compared to 20-gauge probes). Xenon and LED light sources of new generation surgical vitrectomy systems contributed to solution of the problem, and chandelier endoillumination systems for bimanual surgery were proposed to help with difficult manipulations in retina.

The combination of phacoemulsification and vitrectomy has theoretical advantages such as maintaining clear visualization during surgery and relieving the need for a second cataract surgery after vitrectomy. In most of the published studies on combined surgeries in DR complications[14,15], vitrectomy was performed using the traditional 20-gauge technique. In this regard, it is relevant to study the results of combined phacoemulsification and mini-invasive (23-gauge and 25-gauge) vitrectomy in DR.

Vascular endothelial growth factor (VEGF) is a specific regulator of mitogenic activity and vascular conductance of endothelial cells and plays a key role in the development of

[12] Eckardt, C. Transconjunctival sutureless 23-gauge vitrectomy // Retina, – 2005; – vol.25: – p.208– 211.

[13] Oshima, Y. A 27-gauge instrument system for transconjunctival sutureless microincision vitrectomy surgery / Y. Oshima, T. Wakabayashi, T. Sato [et al.] // Ophthalmology, – 2010; – vol.117: – p.93-102.

[14] Lahey, J. M., Francis R.R., Kearney J.J. Combining phacoemulsification with pars plana vitrectomy in patients with proliferative diabetic retinopathy // Curr Opin Ophthalmol, – 2004, – vol.15: – p.192-196.

[15] Rivas-Aguino, P. Pars plana vitrectomy, phacoemulsification and intraocular lens implantation for the management of cataract and proliferative diabetic retinopathy: comparison of a combined versus two-step surgical approach / P. Rivas-Aguino, R.A. Garcia-Amaris, M.H. Berrocal [et al.] // Arch Soc Esp Oftalmol, – 2009, – 84, – p.31-38.

angiogenesis and macular edema in DR[16]. Currently, several drugs (bevacizumab, ranibizumab, aflibercept), that inhibit VEGF activity at different stages (VEGF protein synthesis, binding to VEGF receptors), are used in the treatment of diabetic macular edema and intraocular neovascularization of diabetic origin. There are reports of beneficial effect of preoperative use of anti-VEGF agents for the prevention of intraoperative and early postoperative hemorrhage in DR[17], however, their benefits have been questioned in some studies[18].

Mini-invasive vitrectomy is a promising surgical technique for complications of DR, but some aspects of it require further study. This includes, first of all, re-assessing the indications and timing for the operation, determining the risk factors, affecting the results of the operation and studying the clinical efficacy of the various latest surgical technologies.

Object of research. In the present study, the results of vitrectomy performed in 502 eyes of 433 patients with various complications of diabetic retinopathy in 2009-2015 at the Department of Diabetic Eye Disease of the National Ophthalmology Center named after Academician Zarifa Aliyeva were analyzed. The control group included 78 eyes (78 patients), where vitrectomy was recommended for complications DR, the surgery was not performed for various reasons. The patients included 193 men (44.6%) and 240 women (55.4%). Inclusion criteria of the the study: one or several complications of diabetic retinopathy resistant to laser and

[16] Aiello, L.P. Vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders / L.P. Aiello, R.L. Avery, P.G. Arrigg [et al.] // N Engl J Med, – 1994; – v.331; – p.1480–1487.

[17] Rizzo, S. Injection of intravitreal bevacizumab (Avastin) as a preoperative adjunct before vitrectomy surgery in the treatment of severe proliferative diabetic retinopathy (PDR) / S. Rizzo, F. Genovesi-Ebert, E. Di Bartolo [et al.] // Graefes Arch Clin Exp Ophthalmol, – 2008; – 246(6), – p.837-842.

[18] Lo, W.R. Visual outcomes and incidence of recurrent vitreous hemorrhage after vitrectomy in diabetic eyes pretreated with bevacizumab (avastin) / W.R. Lo, S.J. Kim, T.M. Aaberg, Sr. [et al.] // Retina, – 2009, – v.29, – p.926-931.

pharmacologic treatment (intravitreal / subhyaloid hemorrhage, or opacity, tractional retinal detachment, tractional-rhegmatogenous retinal detachment, diabetic maculopathy, asteroid hyalosis, progressive fibrovascular proliferation, preretinal hemorrhage), of all age groups, both sexes, exclusion criteria: eyes operated previously for complications of diabetic retinopathy.

Purpose of the study:

Improving the efficiency of surgical treatment of complications of diabetic retinopathy by using the latest technological innovations in ophthalmic surgery, including small incision pars plana vitrectomy.

Research tasks:

1. Revision of existing classifications of diabetic retinopathy using modern diagnostic tools (spectral domain optical coherence tomography, ultrasound examination), revision of indications for surgery.
2. Study of the anatomical and functional outcomes of mini-invasive vitrectomy (23 and 25-gauge pars plana vitrectomy) for complications of diabetic retinopathy.
3. Study of the efficacy of combined mini-invasive surgery (phacoemulsification and mini-invasive vitrectomy) for complications of diabetic retinopathy.
4. Study of the results of removal of the internal limiting membrane during mini-invasive vitrectomy in patients with diabetic retinopathy.
5. Study of the results of use of anti-VEGF agents as an adjuvant before mini-invasive vitrectomy in patients with diabetic retinopathy.
6. Study of the results of the use of various tamponading agents (silicone oil, gas and air) in mini-invasive vitrectomy in eyes with diabetic retinopathy.
7. Study of the frequency and risk factors of complications after mini-invasive vitrectomy in patients with diabetic retinopathy,

assessment of the effectiveness of preventive and therapeutic measures.

8. Setting indications for 25-gauge pars plana vitrectomy, study of the results of surgical interventions.
9. Development of an algorithm for surgical treatment and observation in complications of diabetic retinopathy.

Research methods. The present study is a clinical investigation using both retrospective and prospective research methods. Diagnostic methods included visometry, tonometry, biomicroscopy, fundoscopy, ultrasound examination, optical coherence tomography, microperimetry. Surgical interventions included vitrectomy (23 and 25 gauge), endolaser photocoagulation, internal limiting membrane peeling, cataract phacoemulsification and IOL implantation, intravitreal anti-VEGF injection, and silicone oil removal. Statistical data were entered into a database in the SPSS software (IBM SPSS Statistics 20.0, IBM Corp., USA) and were processed in an automated manner. Three types of variables were used: nominal, ordinal, and continous variables. Average and standard deviation (M ± SD) were calculated for continous variables. Shapiro-Wilk test, Student t-test, Mann-Whitney U test, Wilcoxon test, Pearson $\chi 2$ test, Fisher correction, one-way ANOVA test, post-hoc (Scheffe, Tukey and Bonferroni tests), Spearman ρ test, logistic regression analysis, Kaplan-Meyer survival analysis, Cox-Mantel or log-rank tests were applied. The statistical reliability rate (p) was taken to be 0.05, as accepted in medical studies, and the results were considered statistically significant when the reliability rate p was less than 0.05. The main evaluation criterion was based on the analysis of visual acuity of the operated and the control eyes. Analysis of visual acuity was performed using LogMAR (logarithm of the minimum angle of resolution) units.

The applicant's personal contribution to the research. In all clinical cases included in the dissertation, diagnostic procedures and surgeries, statistical processing and analysis of the collected data were carried out entirely by the author.

Scientific novelty of work

1. Indications for surgical treatment in diabetic retinopathy are re-classified on the basis of modern research methods (ultrasound and OCT), rare forms of the disease requiring surgical treatment are described.
2. The status of the posterior hyaloid membrane in diabetic retinopathy was re-classified and its prognostic significance for vitrectomy was investigated in the dissertation.
3. The early and long-term results of mini-invasive vitrectomy in diabetic retinopathy were studied prospectively, the frequencies and risk factors of postoperative complications were cleared.
4. For the first time, the results of vitrectomy in diabetic retinopathy were assessed by microperimetry along with visometry; the dynamics of changes in the sensitivity of the retina after surgery was described.
5. For the first time, OCT features of morphological changes in the macular region after removal of the internal limiting membrane were determined and the results of modified (limited) peeling of the internal limiting membrane were studied in order to minimize postoperative anatomical changes in the macula.
6. On the basis of the obtained data, recommendations have been developed for the optimal timing and optimal surgical technique of mini-invasive vitrectomy in the eyes with diabetic retinopathy complications.

The practical significance of the work

The obtained results may help determine the optimal time and method of surgical treatment in the eyes with diabetic retinopathy, predict and reduce the incidence of intraoperative and postoperative complications, improve the functional outcomes of surgery and reduce disability rate due to complications of diabetic retinopathy.

The dissertation is part of the research plan of the National Center of Ophthalmology named after academician Zarifa Aliyeva (2011-2015), "Improving the treatment of diabetic retinopathy" (State Registration No. 01134008).

The basic concepts for the discussion:

1. Analysis of early and long-term results of mini-invasive (23 gauge and 25 gauge) pars plana vitrectomy for various complications of diabetic retinopathy confirms the anatomical and functional efficiency of the surgery. 25-gauge vitrectomy, giving anatomical and functional outcomes comparable with a 23-gauge vitrectomy, provides greater patient comfort in the postoperative period.
2. Similar anatomical and functional results in the long-term period were obtained after combined surgery (phacoemulsification and vitrectomy) and two-stage vitrectomy and phacoemulsification in phakic eyes with complications of diabetic retinopathy.
3. Removal of the internal limiting membrane during mini-invasive pars plana vitrectomy in the eyes with complications of diabetic retinopathy increases the anatomical success of the surgery, but at the same time causes asymmetric changes in the thickness of the retina in the macular region. Limited removal of the internal limiting membrane instead of the traditional large-area removal, provides similar anatomical results with less changes in macular thickness.
4. Preoperative intravitreal injection of anti-VEGF agents helps to reduce the incidence of intraoperative complications and early recurrent hemorrhages after vitrectomy in the eyes with diabetic retinopathy.
5. The most serious postoperative complications of mini-invasive vitrectomy in diabetic retinopathy are postoperative glaucoma and recurrent hemorrhage into the vitreous cavity. Retention of adhesion between the posterior vitreous body and the retina is a significant risk factor for iatrogenic tear during surgery, intraoperative hemorrhage, early recurrent hemorrhage, and recurrent retinal detachment. Preoperative iris new vessels are a major risk factor for late recurrent hemorrhage.

The practical application of the obtained results. The results of the study are used in the practical work of the Department of Diabetic eye disease of the National Center of Ophthalmology

named after Academician Zarifa Aliyeva. The study materials were also included in the manual on ophthalmology ("Eye Diseases", Baku, 2014), in the program of lectures for residents in the specialty of "Ophthalmology".

Approbation of work. The main concepts of the study were reported at international scientific conferences dedicated to the 87th, 89th, 90th and 95th anniversary of academician Zarifa Aliyeva (Baku, 2010, 2012, 2013, 2018), at the 44th, 46th National Congresses of the Turkish Ophthalmological Society (TOD) (Antalya, Turkey, 2010, 2012), at a joint conference of the Black Sea Ophthalmological Society (BSOS) and the Academy of the European Society of Cataract and Refractive Surgeons (ESCRS), (Tbilisi, Georgia, 2013), at the TbilisiEyeLive live surgery symposium (Tbilisi, Georgia , 2014), at the courses on retinal diseases of the Society of Ophthalmologists of Turkic-speaking Countries (Baku, 2014), at the XIII International Conference of the Egyptian Vitreoretinal Society (Cairo, Egypt, 2015), at the XV EURETINA Congress (Nice, France, 2015), at the I and II Conferences of Retinologists of Azerbaijan (Lankaran 2016, Baku, 2017), at a scientific conference dedicated to the opening of the branch of the National Center of Ophthalmology named after academician Zarifa Aliyeva (Ganja, 2016), at the international conference "Actual issues of treatment of diseases of the retina and optic nerve - RetinaPodilla 2017" (Vinnitsa, Ukraine, 2017), at the international TROC symposium "Diabetes and the Eye" (Osh, Kyrgyzstan, 2017), at a scientific conference dedicated to the 95th anniversary of academician Zarifa Aliyeva "Modern achievements of health care", (Baku, 2018).

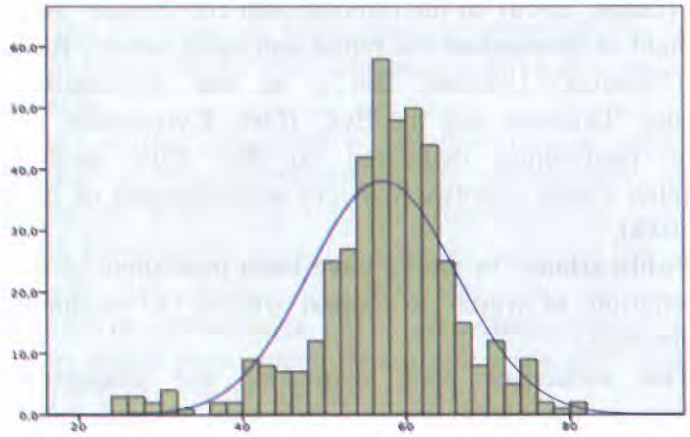
Publications. 34 works have been published on the topic of the dissertation, of which 26 journal articles (17 in domestic, 9 in foreign journals).

The structure and scope of the dissertation. The dissertation is presented on 283 pages of printed text (367.600 characters), consists of an introduction, a literature review, a chapter of the material of methods, 8 chapters of research results, discussion, conclusions and practical recommendations. The list of references

contains 407 sources, of which 4 are in Azerbaijani, 17 in Russian and 386 in English languages. The dissertation is illustrated with 27 figures, 20 graphs and 62 tables.

MATERIAL AND METHODS

This work analyzes the results of vitrectomy performed for various complications of diabetic retinopathy (DR) in 502 eyes of 433 patients in the Department of Diabetic eye disease of the National Center of Ophthalmology named after Academician Zarifa Aliyeva in 2009-2015. Among the patients there were 240 females (55.4%) and 193 males (44.6%). Most of the patients - 96.7% - were patients with type 2 diabetes mellitus (DM). The duration of diabetes in patients with type 1 diabetes was 16.0 ± 6.5 years, in patients with type 2 diabetes - 13.29 ± 7.08 years. Sixty-one patients with type 2 diabetes (14.6%) used oral antiglycemic agents to normalize blood sugar levels, the rest of type 2 diabetes patients and all type 1 diabetes patients used insulin therapy. The level of glycosylated hemoglobin (HbA1c, in %) was 8.27 ± 1.06 in patients with type I diabetes, 7.77 ± 1.04 in patients with type II diabetes ($p > 0.05$). Distribution of treated patients by age is shown in Graph 1.



Graph 1. Distribution of treated patients by age (with an indicator of normality).

History and preoperative examination revealed arterial hypertension in 106 patients (24.5%), severe coronary heart disease (one or more myocardial infarction or surgery for coronary heart disease in the history) in 48 patients (11.1%), 9 patients (2.1%) had a history of stroke. Amputations in the lower extremities due to complications of the diabetic foot were mentioned in the history of 35 patients (8.1%). 4 patients were on hemodialysis due to renal failure (0.9%).

In 69 out of 433 patients, vitrectomy for complications of diabetic retinopathy was performed in both eyes during the follow-up period (138 eyes, 27.5%). In 130 patients (25.0%), the operated eye was the only functional eye.

Examination methods. Standard examination of the patients' eyes included visometry, refractometry, tonometry, biomicroscopy (with a narrow pupil and after pharmacological mydriasis). Fundoscopy was performed using a 90D lens on a slit lamp, and fundus images were recorded using Visucam ProNM camera (Carl Zeiss, Germany). In the eyes with opaque media, (due to cataract or vitreous hemorrhage), the state of the posterior segment was assessed using an ultrasound (B-scan) examination (EZ Scan AB5500, Sonomed, USA).

Optical coherence tomography (OCT). The condition of the vitreoretinal interface, retinal thickness, retinal layers and subretinal area were studied using spectral domain optical coherence tomography (OCT). Cirrus HD device was used for OCT examination (Carl Zeiss Meditec, Dublin, CA, USA). The Macular Cube protocol was used to analyze the topography of the macular area during this examination, and the 5-line HD-Raster protocol to further assess the condition of the retinal layers.

Microperimetry. In some of the observed eyes, microperimetry examination (CenterVue, Padova, Italy) was performed using the MAIA (Macular Integrity Assessment) device to assess the sensitivity of the retina, detect microscotomata and study the fixation features. Patients were examined using the standard Expert Exam protocol. In this test, light is illuminated in a zone at a distance of 10 ° from the central fixation point for 37 points (12 in 3

concentric rings and the center point), and the retinal sensitivity and fixation assessment map was created.

Posterior hyaloid membrane assessment. The condition of the posterior hyaloid membrane was assessed on the basis of ultrasound data (B-scan) during the preoperative study and was re-assessed later during the surgery. Due to the lack of a generally accepted classification of the level of adhesion of the posterior hyaloid membrane to the retina, we used our own working classification to analyze the role of posterior hyaloid membrane in the occurrence of retinal detachment. On this scale, 4 degrees of posterior hyaloid membrane adhesion to the retina in patients with DR were distinguished: 1 - complete detachment of the posterior hyaloid or single point adhesion, 2 - flat adhesion of the posterior hyaloid (area greater than 1 disc diameter) limited by the posterior pole (the periphery is free at 360 °), 3 - sectoral adhesion of the posterior hyaloid on the periphery with a length of less than 2 quadrants (as a rule, nasal adhesion was preserved), 4 - complete or almost complete adhesion of the posterior hyaloid on the periphery and in the posterior pole (more than 2 quadrants of the periphery).

Surgical methods. Intravitreal administration of anti-VEGF agents was performed under sterile conditions in the operating room transconjunctivally in the lower temporal quadrant of the eyeball using a 27-gauge needle, at a distance of 3.5-4 mm from the limbus in phakic eyes and 3 mm from the limbus in pseudophakic eyes. For injection, 0.05 ml (1.25 mg) of bevacizumab (Avastin, Genentech, USA) was used. Antiobiotic eyedrops were administered post-injection for infection prophylaxis.

Cataract extraction technique. Phacoemulsification of cataract with IOL implantation (in 2 steps, combined or after vitrectomy) was performed on a number of the phakic eyes during the study period. In combined cases, cataract phacoemulsification with IOL implantation was performed at the beginning of the surgery. To stabilize the anterior chamber during the posterior vitrectomy, a 10:0 nylon suture was applied to the corneal incision, and to preserve the transparency of the cornea, hydration of the corneal incisions was not performed.

Vitrectomy surgery technique. Operations were performed under local anesthesia with 2% lidocaine or under general anesthesia using Accurus 800 CS or Constellation surgical systems (Alcon, Forth Worth, Tex., USA), a wide-angle visualization system of the posterior segment of the eyeball BIOM 4m (Oculus, Almaniya) under an operating microscope Zeiss Lumera T and Zeiss Lumera 700 (Carl Zeiss, Germany), with an integrated HD camera for video recording. Disposable 23-gauge trocars were inserted into the eye at a 30 ° angle with conjunctival retraction. Vitrectomy started with a core vitrectomy. We used a frequency of 1500-2500 cuts / min., vacuum up to 450 mm Hg. The next step was to release the anterio-posterior traction (*peripheral vitreal rhexis*). To assess the state of the posterior hyaloid, staining with triamcionolone acetonide was performed. The fibrovascular membranes at the posterior pole were segmented and removed with a vitrectomy probe, and if necessary, scissors and serrated forceps were used. If panretinal laser photocoagulation was not performed or was performed partially previously, it was carried out in full during surgery. To ensure complete laser photocoagulation at the periphery, scleral depression was used. In combined cases, at the end of the surgery, a posterior capsulectomy was performed using a vitrectomy probe. BSS (balanced salt solution, Alcon, USA), sterile air, gas, or silicone oil were used to restore the vitreous cavity at the end of the surgery. For the purpose of the gas tamponade, a non-expanding concentration of the gas-air mixture was used (20% for sulfur hexafluoride (SF6) or 14% for perfluoropropane (C3F8)). After gas tamponade, patients were recommended to be in a face-down position for 1 week. In all cases with silicone oil tamponade, 1000 cst silicone oil was used. On eyes with silicone tamponade, 7: 0 absorbable sutures (polyglycolic acid, PGA, MANI, Japan) were applied to close sclerotomies.

Internal limiting membrane (ILM) removal technique. After stopping the infusion, brilliant blue (BBG) was injected into the eye, and the dye was rinsed out after 30 seconds. Then, using a Tano scraper or Eckgardt forceps, the temporal edge of the membrane was lifted and the membrane was removed with forceps. In the standard technique, the membrane was removed between the vascular arcades;

with modified (limited) peeling, the ILM was removed over an area of 1–2 disc diameters around the fovea (Figure 1.).

Figure 1. Limited ILM removal.

Tamponading agents. BSS (Balanced Salt Solution, Alcon, USA), sterile air, gas, or silicone oil were used to restore the vitreous cavity. A non-expansile concentration of sulfur hexafluoride (SF6) or perfluoropropane (C3F8) gases (20% for sulfur hexafluoride and 14% for perfluoropropane) was used for gas tamponade. After gas tamponade, patients were advised to lie down for 1 week. Silicone oil with a viscosity of 1000 cst was used in all cases for the purpose of silicone oil tamponade.

Removal of silicone oil. Silicone oil was removed 3-6 months after the primary surgery, except in special cases. Simultaneous phacoemulsification of cataracts and IOL implantation were performed during removal of silicone oil in the phakic eyes. In order to accelerate the automatic aspiration of silicone oil, a specially designed adapter was attached to the end of the injector, the adapter was placed over the conjunctiva to create a vacuum, and in this way, the diameter of the silicone aspiration tube was equal to the inner diameter of the cannula.

Statistical research methods. All collected data were entered into a database, created in the SPSS software (IBM SPSS Statistics, IBM Corp., USA) and automated calculations were performed. Three

types of variables were used: categorical, ordinal, and quantitative variables. Mean and standard deviation (M ± SD) was calculated for quantitative variables. In the large groups of variables (n> 30-40), the normality test was not performed due to the limited effect of the distribution on the results. The Shapiro-Wilk test was used to determine the normality of continuous data distribution. For continuous quantitative variables, when comparing results in independent groups, the Student t-criterion was used if the distribution of data was normal and the Mann-Whitney U (Wilcoxon rank-sum test) test if the distribution of data was not normal. When comparing results in paired-samples, Student t-criterion was used if the distribution of data was normal, and Wilcoxon signed-ranks test was used if not. The Pearson $\chi 2$ criterion was used to compare nominal and ordinal variables. Fisher exact correction was applied for small groups. The One-Way ANOVA test was used to determine the difference between the parametric means between two or more groups. If a reliable difference was found between the groups, then post-hoc (Scheffe, Tukey, and Bonferroni) tests were used to make binary comparisons between the different groups. The Pearson's rank correlation coefficient (Pearson's r coefficient) and the Spearman ρ test (Spearman's rank correlation coefficient ρ) were used to determine the relationship between the two different variables.

If one of the variables was binary and the others were different, then a logistic regression analysis was performed to identify risk factors. Kaplan-Meier survival analysis was used to study the relationship between time and event (probability of cataract surgery after vitrectomy, probability of late hemorrhage, etc.). Cox-Mantel or log-rank tests were used to study the difference in event probability in different groups.

Analysis of visual acuity was performed with LogMAR (logarithm of the minimum angle of resolution) units, as recommended in recent scientific literature[19]. During the examination, the results of visual acuity were calculated in decimal

[19] Holladay, J.T. Visual acuity measurements // J Cataract Refract Surg. – 2004; – v.30: – p.287-290.

system, then converted into LogMAR system using a special conversion table and placed in a database and statistical calculations were performed. The counting of fingers in front of the eye was taken as 0.01 (LogMAR 2.0), and the detection of hand movements in front of the eye was taken as 0.001 (LogMAR 3.0). The light perception and the absence of light perception were excluded from the calculations because they were not true visual functions but only in response to stimuli, and the results were recorded separately.

The statistical significance rate (p) was taken to be 0.05, as accepted in medical studies, and was recorded as $p < 0.001$ if p was less than 0.001. The results were considered statistically significant when the reliability rate p was less than 0.05.

RESULTS OF THE STUDY

Chapter III. Main indications for vitrectomy in diabetic retinopathy, anatomical and functional data of the operated eye. In 189 (37.7%) of the 502 eyes that underwent mini-invasive vitrectomy, the main indications for surgery were non-absorbable intraocular hemorrhage and vitreous opacities (Table 1). Hemorrhages were further subdivided into intravitreal / subhyaloid (or retrohyaloid) and preretinal hemorrhages. Intraocular hemorrhage (vitreal / subhyaloid) was found in only 161 eyes (32.1%). Intravitreal hemorrhage was recorded in 138 eyes (27.5%). In 13 eyes (2.6%), hemorrhage occurred in the retrohyaloid area after subtotal detachment of the posterior hyaloid, and in 10 eyes (2.0%) both in the vitreous and in the subhyaloid area. Severe preretinal or premacular hemorrhage (in eyes with posterior hyaloid adhesion) was the main indication for vitrectomy in 22 eyes, accounting for 4.4% of all indications for vitrectomy. Vitreous opacities (0.6%) as a result of old hemorrhage in 3 eyes was indicated for vitrectomy. Asteroid hyalosis in 3 more eyes was the main indication for vitrectomy surgery in the background of DR.

Table 1.

The main indications for mini-invasive vitrectomy in complications of diabetic retinopathy

Indications for surgery	n	%
Vitreal / subhialoid hemorrhage or opacity	164	32.7
Tractional retinal detachment	77	15.3
Tractional retinal detachment, with hemorrhage	162	32.3
Tractional-rhegmatogenous retinal detachment	28	5.6
Diabetic maculopathies	39	7.8
Preretinal hemorrhage	22	4.4
Progressive fibrovascular proliferation	7	1.4
Asteroid hyalosis	3	0.6
Total	502	100.0

Tractional retinal detachments were relatively prevalent among the indications for vitrectomy (239 eyes, 47.6%). Depending on the involvement of the fovea in the process, these eyes are divided

into 2 major groups: fovea-off and fovea-on detachments. Fovea-off detachments were observed in 129 eyes (25.7% of all eyes), and extrafoveal detachments were observed in 110 eyes (21.9%). Fresh intravitreal / retrohyaloid hemorrhages have been reported in some of the eyes operated on for retinal detachments. These hemorrhages were observed in about half of the eyes with foveal involvement - 47.6%, and in most eyes without foveal detachment - 86.4%. In general, fresh intraocular hemorrhages were observed in 157 (65.9%) of the eyes operated on for tractional retinal detachment.

The indication for vitrectomy in 28 eyes (5.6%) was combined tractional-rhegmatogenous retinal detachment. Tractional tear was detected in 23 eyes (82.1%) before surgery, and in 5 eyes (17.9%), tractional-rhegmatogenous was diagnosed based on other clinical signs and the tear was discovered during surgery. In 5 cases (17.9%) the fovea was on, and in other cases it was detached. In addition, vitreal hemorrhage was observed in 9 eyes (32.1%), subhyaloid hemorrhage in 2 eyes (7.1%), and subretinal hemorrhage in 7 eyes (25.0%). In 25 (89.3%) of these cases, the clinical picture corresponded to the classical tractional-rhegmatogenous characteristics, but in 3 eyes rare forms of detachment due to atypical localization of the tear were observed. In 2 eyes, traction by fibrovascular membranes caused a peripheral tear in the zone of lattice degeneration and rhegmatogenous detachment. In one eye, where a large retinoschisis was observed in the background of proliferative DR, traction of the epiretinal membrane in the periphery led to a tear in the inner layer of retinoschisis and a combined tractional-rhegmatogenous detachment.

Active fibrovascular proliferation in the posterior pole, resistant to treatment, was the main indication for vitrectomy in 7 eyes (1.4%).

A total of 39 eyes (7.8%) underwent vitrectomy due to changes in the macular area. The majority of these eyes (28 eyes, 5.6%) were with diabetic macular edema (DME). Edema was tractional in all eyes (26 eyes) operated on with a diagnosis of DME, except for 2 eyes with non- tractional DME. Two types of traction in DME were also distinguished. Edema due to tangential macular traction was observed in 17 eyes (65.4%) and vitreofoveolar traction in 9 eyes (34.6%). Different types of macular holes were the second group to undergo mini-invasive

vitrectomy. Vitrectomy was performed in 3 eyes (0.6%), where traction from the fibrovascular membrane resulted in full-thickness macular hole. Vitrectomy was performed also in 6 eyes (1.2%) with tangential tractional edema and lamellar hole, and in 2 eyes with pseudomacular hole and parafoveal edema (0.4%). Preoperative iris neovascularization was observed in 1 eye with macular hole.

Preoperative iris neovascularization was noted in 39 operated eyes, and 121 eyes had previously received anti-VEGF injections.

Chapter IV. Anatomical and functional outcomes of mini-invasive vitrectomy for complications of diabetic retinopathy. The mean follow-up period of patients was 26.99 ± 23.04 months (range 1-114 months). During the observation period, 38 out of 433 patients confirmedly died. Overall, in 70 of the 502 eyes operated on, the follow-up period was less than 6 months due to the patients' death or failure to continue the follow-up. The anatomical results of the operation were assessed on the basis of fundus biomicroscopy, B-scan and OCT after at least 6 months of observation. At the last visit, retina was attached in most eyes (369 eyes, 85.4%) without endotamponade. Another 57 eyes (13.2%) had retinal attachment under silicone oil, and only 6 eyes (1.4%) had postoperative retinal detachment (with or without tamponade). The observation period in 371 eyes was 12 months or more. In the last examination in these eyes, 86.8% of cases, the retina was attached without tamponade, in 12.6% it was attached under silicone oil, and detached in 1.6% of cases.

In 24 eyes of 23 patients (10 males, 13 females), absorption of subretinal fluid (SRF) was studied using OCT after vitrectomy performed for macula-off tractional retinal detachment. The study included only patients with successful anatomical results and eyes which completed follow-up with OCT examinations for at least 12 months. In 11 eyes (45.8%) the duration of macular detachment was from few days to 1 month, in other cases this period was more than 1 month. Active aspiration of subretinal fluid from drainage retinotomy was performed outside the large arcades in 13 eyes. In all eyes, the retina was attached clinically after surgery. Silicone oil was removed without complications in all 13 eyes that underwent silicone oil tamponade.

The preoperative height of subretinal fluid in the macula was 361.56 ± 239.27 μm (between 112-900 μm). The central foveal thickness (CFT) was 692.89 ± 265.18 μm (between 290-1200 μm) before surgery. Residual subretinal fluid was detected in all eyes after surgery on OCT. (Fig.2). Residual fluid decreased over time and was absorbed in all eyes without the need for additional intervention. The residual SRF absorption period was in average 7.78 ± 3.49 months after vitrectomy (range 3-19 months). Residual fluid levels decreased during the follow-up period from 1 to 12 months ($p < 0.001$, Friedman test).

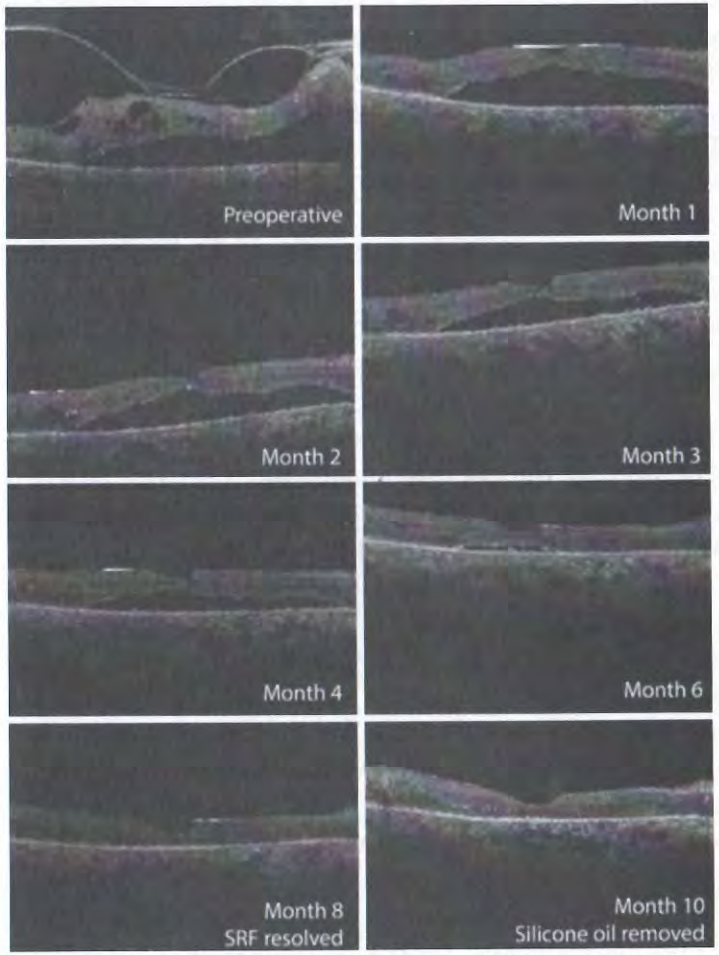
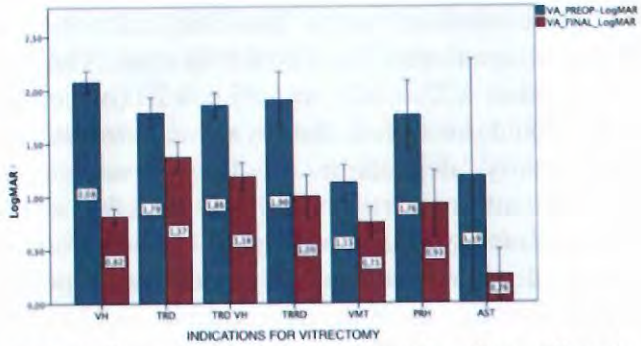


Figure 2. Change of SRF level on OCT examination.

The complete absorption time of SRF was not statistically significantly different between relatively new and old macular detachments (8.18 ± 2.27 and 7.54 ± 4.23 months, respectively, $p = 0.652$). Multifactorial logistic regression analysis showed that the only reliable risk factor for maintained SRF after 6 months was non-drainage ($B = 2.62$, risk rate = 13.74, $p = 0.04$).

The mean BCVA (in LogMAR units) improved from preoperative 1.54 ± 0.75 to 0.99 ± 0.58 after 6 months and increased further after 1 year to 0.91 ± 0.67. ($p = 0.005$, Friedman test). No reliable correlation has been established between SRF full absorption time and final visual acuity ($rs = -0.233$, $p = 0.273$).

Functional outcomes of mini-invasive vitrectomy for various complications of diabetic retinopathy. Eyes observed for at least 6 months were selected to study the results of vitrectomy during DR complications. At the last examination of these eyes, BCVA improved with LogMAR units from 1.84 ± 0.76 to 0.93 ± 0.64 ($p < 0.001$).



Graph 2. Dynamics of visual acuity after vitrectomy in different groups.

Overall, 371 (85.9%) of the 432 eyes that completed a follow-up period of 6 months or more had improved visual acuity, 36 (8.3%) had no change in visual acuity, and only 25 (5.8%) had deterioration of BCVA.

The mean duration of follow-up in the eyes, operated for non-absorbing hemorrhages in the vitreous and / or subhyaloid space was

26.16 ± 22.90 months. The average BCVA improved from 2.13 ± 0.72 to 0.79 ± 0.54 after surgery for non-absorbing hemorrhages in the vitreous / subhyaloid space in eyes (142 eyes) who completed 6 months or more of observation. ($p < 0.01$). During the follow-up period, improvement of visual acuity was observed in the absolute majority of eyes included in this group - 137 eyes (96.7%), visual acuity deteriorated only in 2 eyes (1.4%). The follow-up period for eyes undergoing microinvasive vitrectomy for severe premacular hemorrhage was 23.95 ± 21.05 months, and 17 out of 22 eyes completed a 6-month follow-up period. During the last examination, improvement of visual acuity was noted in 14 of these eyes (82.4%) and deterioration in 3 eyes (17.6%). The mean BCVA was very low before surgery (1.75 ± 0.59), and in the last examination it improved significantly and was 0.96 ± 0.73.

A total of 239 microinvasive vitrectomies were performed due to tractional detachment. The mean observation period of patients was 27.46 ± 23.49 months. In 203 of the operated eyes, the observation period was 6 months or more. In 157 (77.3%) of these eyes, visual acuity increased at the last visit, did not change in 28 (13.8%) eyes, and deteriorated in 18 (8.9%) eyes. The mean visual acuity improved from 1.77 ± 0.75 to 1.05 ± 0.70 (in LogMAR units, $p < 0.001$). It should be noted that eyes with retinal detachment differed significantly depending on the presence of macular involvement and intraocular hemorrhage. In the eyes macular detachment, visual acuity was significantly lower before vitrectomy (1.79 ± 0.80), and it improved in the postoperative period (1.26 ± 0.75, $p < 0.001$). Overall, visual acuity improved in 67 (65.7%) of the 102 eyes, did not change in 20 eyes (19.6%), and deteriorated in 15 eyes (14.7%), included in this group with follow-up period of 6 months or more after surgery. After 6 months or more of follow-up in 100 of the 110 eyes with extrafoveal detachment, visual acuity improved in 89 (89.0%) eyes, remained unchanged in 8 eyes (8.0%), and deteriorated in 3 eyes (3.0%). The mean visual acuity in this group of eyes improved from 1.76 ± 0.71 to 0.87 ± 0.58 ($p < 0.001$). Examination of the eyes with and without detachment of the fovea shows that the preoperative visual acuity did not differ significantly

between the two groups ($p = 0.771$). However, the final visual acuity was higher in the group where the fovea was on before surgery ($p < 0.001$).

Microinvasive vitrectomy was performed in 28 eyes due to tractional-rhegmatogenous retinal detachment, the average follow-up period was 25.71 ± 14.72 months. At last visit, BCVA improved in 24 of (85.7%) of the eyes, remained unchanged in 3 eyes (10.7%) and deterioration was observed in 1 eye (3.6%). The mean visual acuity improved from 1.86 ± 0.64 to 1.04 ± 0.68 ($p < 0.001$, Wilcoxon test).

Among the various types of diabetic maculopathies that underwent microinvasive vitrectomy surgery, the largest group consisted of eyes with tractional macular edma (26 eyes). Observations were made in 22 of these eyes for 6 months or more, and at the last examination, BCVA was improved in 21 eyes (95.5%). Visual acuity did not change only in 1 eye after surgery. The mean visual acuity improved from 1.36 ± 0.68 to 0.76 ± 0.44 ($p < 0.001$, Wilcoxon rank test).

Among the different groups divided by vitrectomy indications, the final vision was higher in the vitreous hemorrhage and vitreomacular traction groups (Graph 2.). Subsequent aposterior Tukey analysis showed a reliable difference between the final functional outcome of eyes with vitreous / subhyaloid hemorrhage or opacity and with retinal detachment (without or without hemorrhage) ($p = 0.002$ and $p = 0.003$, respectively). From other groups, a reliable difference was found between eyes operated on for vitremacular traction and eyes operated on for retinal detachment ($p = 0.039$).

The mean observation period for 78 eyes of 78 patients included in the control group was 28.22 ± 16.21 months (12-77 months). At the end of this period, improvement of BCVA was observed in only 8 eyes (10.3%), it did not change in 23 eyes (29.5%), and deteriorated in 47 eyes (60.2%).

Long-term results of mini-invasive vitrectomy. 53 eyes of 44 patients were observed for 5 years (60 months or more). The mean follow-up period of these patients was 77.7 ± 14.9 months (range 60-114 months). At the end of this period, the retina was attached in all

eyes (6 eyes, 11.3%, under silicone oil). The mean visual acuity (with LogMAR units) improved from preoperative 1.66 ± 0.76 to 0.84 ± 0.63, at 1 year after surgery ($p < 0.001$). The improvement in visual acuity was maintained after 5 years, and the mean visual acuity was 0.85 ± 0.68 at the end of the observation period ($p < 0.001$ compared to preoperative 1.66 ± 0.76). At the same time, there was no difference between the mean values of visual acuity after 1 year and 5 years ($p = 0.117$). At the end of the observation period, visual acuity improved in 48 eyes (90.6%) compared to preoperative, in 4 eyes (7.5%) it did not change, and in 1 eye (1.9%) it was deteriorated. At the same time, visual acuity was 0.1 and higher in 39 patients (73.5%).

Chapter V. Outcomes of combined mini-invasive surgery (phacoemulsification and pars plana vitrectomy) in complications of diabetic retinopathy. Of the 502 eyes (433 patients) with various complications of diabetic retinopathy, who underwent mini-invasive (23 gauge and 25 gauge) pars plana vitrectomy, 61 (12.2%) were pseudophakic, and the remaining 441 (87.8%) were phakic. In 217 out of 441 eyes (49.2%, 200 patients) phacoemulsification, IOL implantation and mini-invasive vitrectomy were performed in the same case (combined group), and in the other 224 eyes (50.8%, 203 patients) only mini-invasive vitrectomy was performed for the first time (control group). In addition, 11 patients had combined surgery in one eye and only vitrectomy in the other eye.

The duration of the primary surgery (phacoemulsification and vitrectomy group) in the combined group was 72.89 ± 18.13 minutes, and in the control group (vitrectomy group) was 60.18 ± 15.47 minutes ($p = 0.002$). Significant differences in intraoperative pupil size were observed between the two groups. At the beginning of the combined operation, the pupil diameter was 6.82 ± 1.82 mm, and at the end of phacoemulsification it was 5.21 ± 1.12 mm. In the control group, where vitrectomy was performed only, the size of the pupil at the beginning of the operation was 7.23 ± 0.99 mm, so the diameter of the pupil immediately before the vitrectomy was significantly

different between the two groups ($p < 0.001$). Edema of the cornea requiring deepitelization during surgery was recorded in 6 eyes in the combined group (1.8%) and in 2 eyes (0.9%) in the phakic group. In the postoperative period, significant corneal edema was noted in 10 (4.6%) in the combined group and in 2 eyes (0.9%) in the control group. In the combined group, postoperative hypertension (12 eyes, 5.5%) was more commonly associated with an inflammatory reaction in the anterior chamber. In the eyes of vitrectomy alone, varying degrees of postoperative hypertension were observed in 18 eyes (8.5%). In the anterior chamber, fibrinous inflammatory reaction was observed in 12 eyes (5.5%) in the combined group, and sterile hypopyon was recorded in 2 eyes (0.9%). In the control group, fibrinous inflammatory reaction was observed in only one eye (0.5%). Bacterial endophthalmitis was recorded in 1 eye after combined surgery (0.5%), infection was controlled after repeated surgery and intravitreal antibiotic injection.

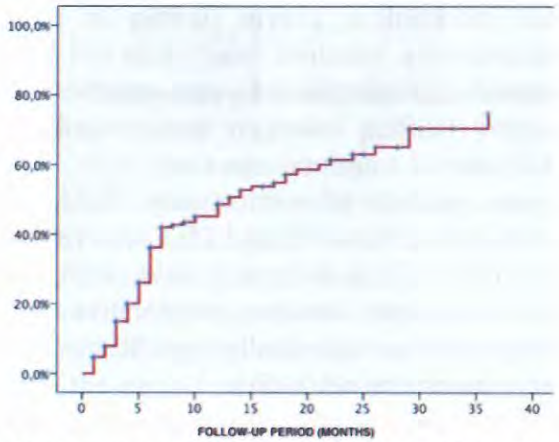
At 1 year and more after vitrectomy, BCVA in the combined group improved from 1.95 ± 0.75 to 1.00 ± 0.91 (in LogMAR), in the control group from 1.75 ± 0.71 to 1.03 ± 0.76 (in both cases, $p < 0.001$ within the group between preoperative and postoperative BCVA, but there was no statistically significant difference between final results in two groups, $p > 0.05$).

The results showed that the final visual acuity was more closely related to the indication for surgery. Visual acuity in eyes with vitreous hemorrhage increased from 2.14 ± 0.72 to 0.72 ± 0.36 ($p < 0.001$) in the combined group, and from 1.99 ± 0.67 to 0.74 ± 0.55 in the vitrectomy only group ($p < 0.001$). There was no statistically significant difference between the two groups in respect to the final result ($p = 0.927$). Similar result was observed, when the main indication for surgery was the tractional retinal detachment (final vision was 1.38 ± 0.79 and 1.28 ± 0.89 in the main and control groups, respectively, $p = 0.635$).

Combined phacoemulsification and vitrectomy resulted in a decrease in the total number of surgeries performed on the patient's eyes. During the observation period, the number of surgeries in the combined group was 1 (74.6%) in 167 eyes, 2 (21.4%) in 48 eyes, 3

or more in 9 eyes (4.0%) (total 292, average number 1.30) . In the control group, 1 surgery was performed on 101 eyes (46.5%), 2 surgeries on 95 eyes (43.8%), 3 or more surgeries on 21 eyes (9.7%) (total 362, average number 1.67) (Pearson $x^2 = 23.62$, $p < 0.001$).

Cataract surgery was performed on 96 (45.5%) of the 211 phakic eyes during the observation period. The mean time between vitrectomy and cataract surgery was 17.85 ± 1.19 months. On the Kaplan-Meyer analysis (Graph 3), the rate of cataract surgery was 36.2% at 6 months, 48.6% at 1 year, 63.1% at 2 years, and 74.7% at 3 years.

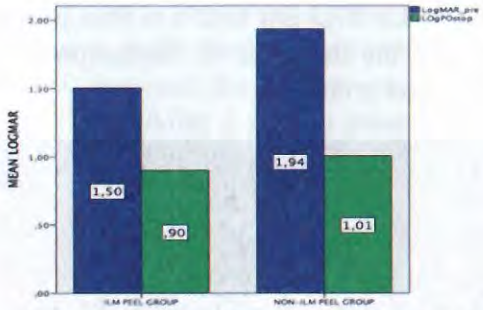


Graph 3. Frequency of cataract surgery after vitrectomy (Kaplan-Meyer analysis).

Chapter VI. Results of internal limiting membrane peel during mini-invasive vitrectomy surgery in diabetic retinopathy. In order to study the results of peeling of the internal limiting membrane (ILM) during vitrectomy for complications of diabetic retinopathy, the results of surgery on 381 eyes of 328 patients were analyzed. ILM was removed during vitrectomy in 149 eyes of 127 patients, and was left intact was in 232 eyes of 201 patients. The observation period ranged from 6 months to 7 years.

Improvement in visual acuity was observed in both groups after surgery (Graph 4). However, there was a significant difference

between the two groups in the number of repeated manipulations in retina. Only 5 (3.6%) of the 149 eyes in the ILM peel group required additional retinal surgery, where 48 (20.7%) of the 232 eyes in the non-ILM peel group had repeated retinal manipulations ($p < 0.001$). At the same time, further BCVA improvement was achieved in only 32 (66.7%) of the 48 eyes ith repeated manipulations.



Graph 4. Visual acuity change in ILM peel and non-peeling group

Twelve months after surgery, the inner temporal, central, and inner nasal thicknesses of the macula in ILM peeled eyes and non-peeled eyes were measured by OCT and compared. Temporal macular thickness (279 ± 51.9 μm) in ILM peeled eyes was thinner than in non-ILM peeled eyes (332 ± 93.8 μm, $p = 0.002$). The thickness of the central and inner nasal layers did not differ significantly between two groups (in both cases $p > 0.05$).

Table 2.
Thickness of macular areas (in μm) 12 months after vitrectomy

	Eyes with peeled ILM (n = 59)	Eyes with intact ILM (n = 30)	p
Internal temporal	279 ± 51.9	332 ± 93.8	**0.002**
Fovea	285 ± 96.6	288 ± 120.6	0.936
Internal nasal	341 ± 99.4	358 ± 107.8	0.496

In the vitreomacular traction group, it was possible to measure the thickness of the retina before surgery. In these eyes, 1 year after

vitrectomy and ILM peel, all thicknesses of the inner ring of the macula were reduced by OCT examination. The internal temporal thickness of the macula decreased from 464 ± 97.7 μm to 295 ± 43.1 μm (p <0.001), and the thickness of the foveolar zone decreased from 520 ± 167.9 μm to 292 ± 78.7 μm (p = 0.001), the internal nasal thickness of the macula decreased from 495 ± 191.8 μm to 377 ± 102.5 μm (p = 0.007) (Figure 3.). In 7 eyes without ILM peel, only foveal thickness decreased significantly (from 498 ± 87.3 μm to 296 ± 90.8 μm, p = 0.014), other parameters, especially the thickness of the temporal macula, changed less than in the ILM peel group.

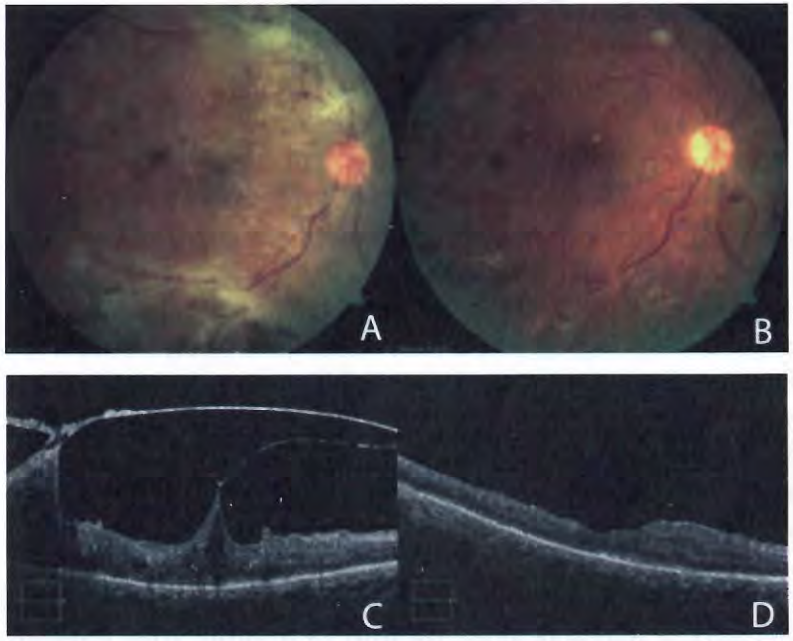


Figure 3. Patient S., 46 years old, right eye. A. Epiretinal membrane before surgery. B. The fundus after surgery (after vitrectomy and ILM peeling). C. Vitreomacular traction on preoperative OCT examination (thickness of the fovea 1390 μm), D., 12 months after surgery – decrease in internal temporal (254 μm) and foveolar (239 μm) thickness, increase in nasal thickness (342 μm).

Because the other eyes of the patients did not meet the criteria for healthy eyes, the results of macular thickness after ILM peeling were compared with normative data from the literature. T. Liu et al.

found that in patients without retinopathy, the internal temporal thickness of the macula measured with the Cirrus HD OCT device was 313.4 ± 18.5 μm[2020], which was considerably higher than the values we obtained after ILM peel (295 ± 43.1 μm, p = 0.002). Nasal (315.9 ± 18.8 μm) and central foveolar thickness (258.5 ± 21.6 μm) in the literature did not differ significantly from our results (341 ± 99.4 μm, p = 0.180 and 285 ± 96.6 μm, p = 0.251, respectively).

In order to minimize anatomical changes in ILM peeled eyes, membrane peeling was performed in restricted manner (less than 2 disc diameters) in 20 eyes and the anatomical features of the macula were studied 1 year later. After 1 year in these eyes, the thickness of the internal temporal macula was 323 ± 56.0 μm, the fovea was 257 ± 95.5 μm, the thickness of the inner nasal macula was 357 ± 66.8 μm, and there was no statistical difference between the thickness of the temporal and nasal macula (p> 0, 05).

Changes in retinal sensitivity in microperimetry and their correlation with changes in visual acuity in the eyes which underwent vitrectomy and ILM peeling were studied. For this purpose, the results of vitrectomy for vitreomacular traction and microperimetry after ILM peel were analyzed in 55 eyes of 42 patients. According to the Expert exam protocol, microperimetry examination was performed in the central zone of 10 ° before, 1 and 3 months after surgery.

Graph 5. Changes of macular sensitivity and visual acuity after vitrectomy and ILM peeling

[20] Liu, T. A pilot study of normative data for macular thickness and volume measurements using Cirrus high-definition optical coherence tomography / T. Liu, A.Y. Hu, A. Kaines [et al.] // Retina, – 2011 Oct; – v.31(9), – p.1944-1950.

The mean BCVA in LogMAR units ranged from 1.12 ± 0.55 to 1.07 ± 0.77 after 1 month and to 0.66 ± 0.46 after 3 months (Graph 5). After 3 months, vision improvement was statistically significant (p = 0.009). According to the results of microperimetry, macular sensitivity improved from preoperative 15.05 ± 4.96 dB to 16.45 ± 4.85 dB after 1 month and to 17.89 ± 5.15 dB after 3 months. In both cases, the results were statistically significant in comparison with the preoperative data (p = 0.026 and p = 0.003, respectively). A weak correlation was observed between visual acuity and macular sensitivity 1 month and 3 months after surgery (r = -0.59, p = 0.071 and r = -0.584, p = 0.059).

Chapter VII. Results of the preoperative use of intravitreal anti-VEGF agents as an adjunct to mini-invasive pars plana vitrectomy in diabetic retinopathy. The results of intravitreal administration of preoperative anti-VEGF agent (1.25 mg bevacizumab) were studied in 48 eyes which underwent vitrectomy for various complications of DR and received intravitreal anti-VEGF within 1 month before surgery. Control group consisted of 70 eyes, operated at the same time with the similar diagnosis, but without preoperative anti-VEGF injections.

The main indications for vitrectomy in the eyes of the anti-VEGF group were as follows: vitreous cavity and / or subhyaloid hemorrhage - 25 eyes (52.1%), retinal detachment with hemorrhage - 16 eyes (33, 3%), vitreomacular traction with hemorrhage - 1 eye (2.1%), severe preretinal hemorrhage - 3 eyes (6.2%), active fibrovascular proliferation - 2 eyes (4.2%). In the control group, the main indications for vitrectomy were: vitreous cavity and / or subhyaloid hemorrhage - 29 eyes (41.4%), retinal detachment with hemorrhage - 32 eyes (45.7%), vitreomacular traction with hemorrhage - 8 eyes (11.4%), active fibrovascular proliferation - 1 eye (1.4%).

The frequency of intraoperative hemorrhage, which significantly affected the course of the surgery, was 15 (31.2%) in the anti-VEGF group and 36 (51.4%) in the control group (p = 0.030). Intraoperative endodiathermy was administered in only 9 (18.8%) of

the 48 eyes in the anti-VEGF group, and in 27 (38.6%) of the 70 eyes in the non-VEGF group (p = 0.026). In the anti-VEGF group, the surgical time was shorter than in the control group (61.70 ± 18.10 and 67.13 ± 19.41 min, respectively, p = 0.223).

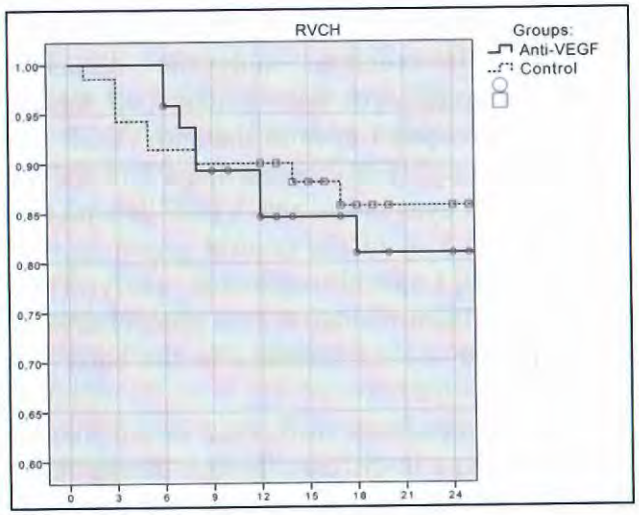
The mean postoperative follow-up was 30.00 ± 20.99 months in the anti-VEGF group and 24.49 ± 10.22 months in the control group (p = 0.060). In order to study the frequency of early postoperative hemorrhage, eyes with silicone oil tamponade were excluded from both groups (8 eyes in the anti-VEGF group and 12 eyes in the control group). Early hemorrhage into the vitreous was recorded in 6 out of 40 eyes in the anti-VEGF group (15.0%) and in 20 out of 58 eyes (35.5%) in the control group (p = 0.038, with Fisher accuracy test). Logistic regression analysis showed that intravitreal anti-VEGF administration as a preoperative adjuvant for vitrectomy reduced the risk of bleeding in the early postoperative period by 3.0 times (p = 0.036).

There was no significant difference in the frequency of late postoperative hemorrhage in different groups during the observation period. Recurrent hemorrhage was observed in 8 eyes (16.7%) in the anti-VEGF group and in 12 eyes (17.1%) in the control group (p = 0.946). In the anti-VEGF group, recurrent hemorrhage was observed on average 9.63 ± 4.14 months, and in the control group earlier - 6.56 ± 5.48 months (p = 0.448).

In addition, the frequency of reoperations for recurrent hemorrhage in the anti-VEGF and control group was compared. During the follow-up period, surgery for recurrent hemorrhage (washing of the vitreous cavity) was performed in 3 out of 48 eyes (6.2%) in the anti-VEGF group and in 8 out of 70 eyes in the control group (11.4%, p = 0.342). In other cases, re-injections of anti-VEGF or observation only were preferred.

During the observation period, a Kaplan-Meyer survival analysis was performed to study the risk of late recurrent hemorrhage into the vitreous cavity (Graph 6) and it was shown that there was no significant difference in recurrent hemorrhage in the two groups for 24 months. After 6 months, 95.8% of the eyes observed in the anti-VEGF group and 91.4% in the control group were free of recurrent

hemorrhage. After 12 months, this figure was 84.6% and 90%, respectively, and after 24 months it was 81.2% and 79.7%. The logarithmic rank (Mantel-Cox) test showed that the difference was statistically non-significant ($\chi 2 = 0.001$; $p = 0.969$).



Graph 6. Risk of bleeding in 24 months in different groups (Kaplan-Meyer analysis)

Prior to surgery, visual acuity was low in both groups (1.66 ± 0.76 and 1.76 ± 0.80, p = 0.519, respectively). Six months after surgery, vision was higher in the anti-VEGF group than in the control group (0.66 ± 0.39 and 0.89 ± 0.47, p = 0.008, respectively). During the 1-year follow-up period, visual acuity in the anti-VEGF group changed slightly (0.67 ± 0.40), in the control group there was an increase in vision (0.75 ± 0.45) and the difference was again invalid (p = 0.310).

Chapter VIII. Comparison of various types of intraocular tamponades during mini-invasive vitrectomy for complications of diabetic retinopathy. At the end of mini-invasive vitrectomy surgery performed on 502 eyes in various complications of DR,

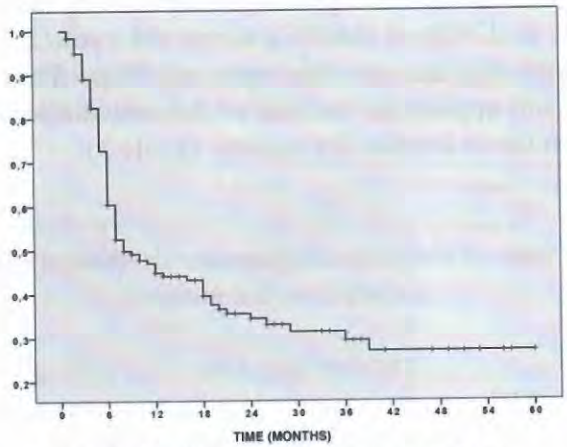
silicone oil was chosen as a primary tamponading agent in 182 eyes (36.3%), gas in 174 eyes (34.3%), air in 113 eyes (22.5%) and BSS solution was applied in 33 eyes (6.6%). The methods of endotamponade applied at the end of surgery differed significantly depending on the indication for surgery (Table 3).

Table 3.

Types of tamponading agents used depending on the indications for surgery

Indications	Silicone oil	Gas	Air	BSS
Vitreal / subhyaloid hemorrhage	6 (3.7%)	55 (33.5%)	75 (45.7%)	28 (17.1%)
Tractional retinal detachment	53 (68.8%)	19 (24.7%)	5 (6.5%)	0 (0.0%)
Tractional retinal detachment / hemorrhage	84 (51.9%)	58 (35.8%)	18 (11.1%)	2 (1.2%)
Tractional-rhegmatogenous retinal detachment	25 (89.3%)	2 (7.1%)	1 (3.6%)	0 (0.0%)
Vitreomacular traction	2 (5.1%)	30 (76.9%)	7 (17.9%)	0 (0.0%)
Preretinal hemorrhage	7 (31.8%)	9 (40.9%)	4 (18.2%)	2 (9.1%)
Asteroid hyalosis	0 (0.0%)	0 (0.0%)	2 (66.7%)	1 (33.3%)
Fibrovascular proliferation	5 (71.4%)	1 (14.3%)	1 (14.3%)	0 (0.0%)

Of the 182 eyes with primary silicone oil tamponade during vitrectomy, 168 (92.3%) had retinal attachment after the first surgery, and 14 eyes (7.7%) had the retina detached. The final anatomical results were better (after repeated surgeries), with retinal attachment in 176 eyes (96.7%) and retinal detachment in only 6 eyes (3.3%). Secondary silicone oil injection was performed in 13 eyes. After repeated surgeries, the retina was reattached in all eyes, and silicone oil was removed in 7 (53.8%) eyes without complications.



Graph 7. Silicone oil removal time (Kaplan-Meyer analysis)

Silicone oil was removed by the end of the observation period in 111 (57.2%) of all 194 silicone oil tamponade eyes, including primary and secondary silicone oil injected eyes. Graph 7 shows the Kaplan-Meyer curve for the removal time of the primarily injected silicone. According to the Kaplan-Meyer analysis, 89.0% of the eyes after 3 months, 60.4% after 6 months, 49.1% after 9 months, 44.8% after 1 year, 34.4% after 2 years, 29.3% after 3 years, 26.9% after 4 and 5 years still had silicone oil tamponade. The average duration of silicone oil removal was 7.7 ± 6.9 months.

After 1 year, improvement of visual acuity was observed in the majority of eyes treated with primary **silicone oil** tamponade (88 out of 132 eyes, 66.7%), visual acuity was unchanged in 26 eyes (19.7%), and visual deterioration was observed in 18 eyes (13, 6%). Average visual acuity (LogMAR) improved from 1.88 ± 0.73 to 1.27 ± 0.74 over 1 year ($p < 0.001$). Eleven of the 12 eyes with secondary silicone oil injection was observed after 1 year. Visual acuity improved in 7 eyes (63.6%), did not change in 3 eyes (27.3%), and deteriorated in 1 eye (9.1%). In general, after 1 year, visual acuity was 0.1 and higher in 3 eyes (27.3%), 0.06-0.1 (18.2%) in 2 eyes, and 0.05 and lower in 6 eyes (54,5%).

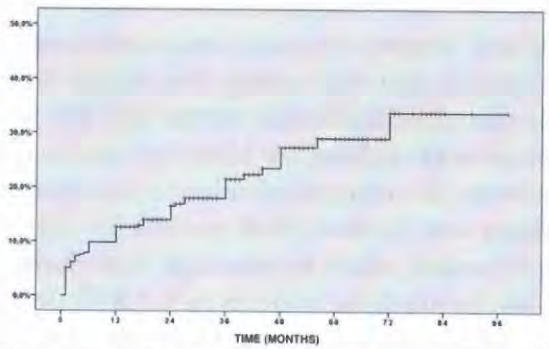
Gas was used in 174 eyes (34.7%) as the primary tamponade. Two types of gas were used for this purpose - hexafluorane (SF_6, non-expanding 20% air-gas mixture) and perfluoropropane (C_3F_8, non-expanding 14% air-gas mixture). Hexafluorane was applied in 140 eyes (80.5%) and perfluoropropane in 34 eyes (19.5%). SF_6 gas was used cases where short-term tamponade was required, with vitreous hemorrhage and upper detachments accompanied by hemorrhage, and C_3F_8 was used in eyes requiring longer-term tamponade, retinal detachment, macular holes, etc. was used. In the majority of operated eyes (169 eyes, 97.1%) at the end of the observation period, the retina was on without a tamponade. During the observation period, recurrent retinal detachment was recorded in 9 eyes, and silicone oil was injected in 8 eyes after repeated surgery.

During vitrectomy for complications of diabetic retinopathy, **air tamponade** was performed at the end of the surgery in 113 eyes, different types of intraocular hemorrhage predominated between these eyes. The largest group was vitreous hemorrhage (66.4%), followed by tractional retinal detachment accompanied by hemorrhage (15.9%). At the end of the observation period, the retina was ttached in 112 eyes (99.1%) and detached in only 1 eye (0.9%). Rhegmatogenous retinal detachment was recorded in 3 of the 113 eyes that underwent mini-invasive vitrectomy and air tamponade for DR complications. Repeated surgery was performed with injection of silicone oil in all 3 eyes, in the last examination in 2 eyes the retina was attached under silicone oil, in 1 eye it was detached.

In a minimally invasive vitrectomy surgery for complications of diabetic retinopathy, the vitreous cavity in 33 eyes was restored with **BSS solution** without any intraoperative complications. The majority of eyes (28 eyes, 84.8%) were operated on for vitreous hemorrhage. At the end of the observation period, the retina was attached in all eyes in this group (33 eyes, 100%).

Chapter IX. Frequency of complications, risk factors and effectiveness of treatment after mini-invasive vitrectomy in diabetic retinopathy. The absolute value of intraocular pressure (IOP) in the first 1 month after primary vitrectomy > 30 mm Hg, or> 5 mm Hg from preoperative level was accepted as early postoperative hypertension. Of the 487 eyes not diagnosed with glaucoma previously, 72 had intraocular hypertension in the early period (14.8%) and 6 eyes had hypotension (1.2%). Early hypertension (14.6%) was found in 6 of the 33 normotensive eyes (18.2%) with preoperative iris neovascularization and in 66 of the 454 eyes without iris neovascularization. ($\chi 2 = 0.375$, $p = 0.54$). Among the causes of early IOP increase were iris bombee in 2 eyes (2.8%), haemolytic glaucoma in 4 eyes (5.6%), and glaucoma due to erythrocyte degeneration in 1 eye (1.4%).

Glaucoma was noted in 70 out of 357 eyes (19.6%) under observation for 1 year or more (average follow-up period 33.75 ± 19.55, maximum 108 months). The rate of newly formed postoperative glaucoma was studied by Kaplan-Meyer analysis (Graph 8), and the relative rate of glaucoma was 9.8% after 6 months, 12.6% after 12 months, 16.5% after 24 months, 21.5 % after 36 months, 27.4% after 48 months, 29.1% after 60 months. The main percentage of postoperative glaucoma (57.14%) consisted silicone oil-dependent glaucoma, glaucoma due to neovascularization in the iris was the second most common (18.57%). IOP elevation of open-angle glaucoma type was observed in 12 eyes (17.1%) without silicone oil tamponade and no anterior segment neovascularization. With the exception of eyes with silicone oil tamponade, the relative incidence of open-angle glaucoma was 5.3% (12 out of 227 eyes). Glaucoma was noted in 35 (29.7%) of the 118 eyes with silicone oil tamponade and where other types of glaucoma were excluded, during the observation period of 34.55 ± 19.02 months.



Graph 8. Cumulative indicator of postoperative glaucoma (Kaplan-Meyer analysis).

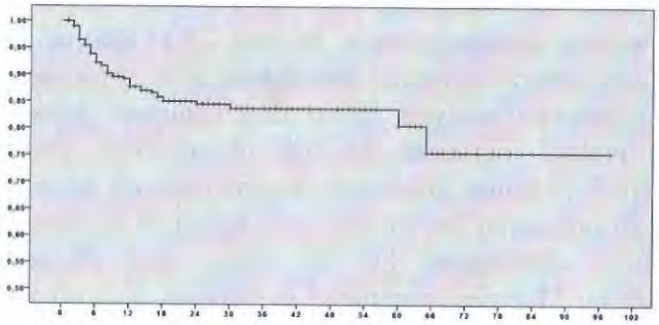
Single-factor regression analysis to determine the main risk factors for postoperative glaucoma showed that preoperative iris neovascularization was not a reliable risk factor for postoperative glaucoma. Among the endotamponading agents, silicone oil injection alone (compared to BSS solution infusion) was found to increase the risk of postoperative glaucoma by approximately 5 times ($p = 0.032$). Silicone oil-related glaucoma has also been linked to the retention time of silicone oil. Thus, for every 1 month of silicone oil tamponade, the risk of glaucoma increased by 1,028 times ($p = 0.027$). Hypertension in the early postoperative period was also found to be a strong risk factor for long-term glaucoma and increased the risk of glaucoma by about 4 times.

In most cases (81.4%) of glaucoma observed in the late postoperative period, it was possible to normalize IOP with the help of hypotensive agents that reduce intraocular fluid production. Ahmed valve implantation was required in 6 eyes (8.6%). IOP was uncontrollable despite treatment in 7 eyes which resulted in loss of visual function.

Frequency, risk factors and treatment of recurrent hemorrhage into the vitreous cavity after pars plana vitrectomy for complications of diabetic retinopathy. Only eyes with primary anatomical success and silicone oil-removed eyes (380 patients, 436 eyes) were included in the study. Two types of postoperative

hemorrhage were distinguished in the study - early and late hemorrhage. Early hemorrhage was considered to occur immediately after surgery, which prevents seeing the details of the fundus and delays the functional rehabilitation of the eye for at least 1 month. Late hemorrhage was defined as bleeding into a clear intraocular cavity after surgery or removal of silicone oil. The mean follow-up period of patients was 24.66 ± 19.90 months (1-108 months). During the observation period, early hemorrhage was observed in 63 eyes (14.4%) and late hemorrhage in 56 eyes (12.8%). In 12 eyes (2.8%), bleeding into the vitreous was observed both early and late. Late bleeding was observed only once in 41 out of 56 eyes (9.4%). In other eyes, bleeding was noted in 2 or more cases. Of the eyes with late-stage hemorrhage, 17 were the only functional eyes. Recurrent hemorrhages were more common in the first 18 months after surgery (Graph 9). The cumulative frequency of recurrent hemorrhages was 7.8% after 6 years, 12.3% after 12 months, 15.0% after 18 months, 15.5% after 24 months, 16.3% after 36 and 48 months, and in 5 years it was 19.3%.

The importance of various local and systemic risk factors for both early and late hemorrhage has been studied separately. For this purpose, a separate multifactorial regression analysis for local and systemic risk factors was performed. Fresh preoperative intraocular hemorrhage increases the risk of premature hemorrhage by about 3 times ($p = 0.015$), anti-VEGF injection performed 1 month before surgery reduces the risk of early hemorrhage by 3 times ($p = 0.039$), partial laser photocoagulation increases the risk of early hemorrhage by 3.5 times ($p = 0.011$). It was also found that early postoperative hemorrhage was less common in eyes with partially adherent hyaloid than in complete adhesion of the posterior hyaloid membrane. Among the intraoperative factors, the risk of bleeding was found to increase 11 and 10 times, respectively, after surgeries completed with gas and air tamponade ($p = 0.024$ and 0.030, respectively). Among systemic factors, only a serious cardiovascular problem (myocardial infarction or heart surgery) increases the risk of early bleeding by 4 times.



Graph 9. Kaplan-Meyer analysis of late hemorrhage after vitrectomy (time in months)

The presence of iris neovascularization in the anamnesis, led to an 8.6-fold increase in the risk of late hemorrhage ($p < 0.001$), and the preoperative new intraocular hemorrhage led to a 3.3-fold increase in the risk of late-stage hemorrhage ($p = 0.015$). it was found that the history of amputation of the lower extremities increased the risk of bleeding by 2.4 times ($p = 0.037$), and negative cardiovascular history (infarction, heart surgery) by 2.8 times ($p = 0.006$).

In most cases (46 eyes, 73.0%) *early hemorrhage* was managed by observation only and the hemorrhage was absorbed spontaneously. Only 17 eyes (27.0%) required washing of the vitreous cavity since earlier rehabilitation was needed. In *late hemorrhages*, only observation was sufficient in 21 eyes (37.5%). Intravitreal anti-VEGF (bevacizumab) injection was performed in 25 eyes (44.6%) to reduce the risk of recurrent hemorrhage, and vitreous lavage was performed in 6 eyes (10.7%) for earlier rehabilitation. In 4 eyes (7.1%), after repeated hemorrhages, silicone oil injection was performed into the vitreous cavity as other measures were not effective.

Primary anatomical success after mini-invasive vitrectomy for DR complications (complete attachment of the retina after the primary surgery) was reported in 459 (95.4%) of 481 eyes, in 21 eyes (4.4%) in the early postoperative period (1 month after surgery) partial or complete rhegmatogenous retinal detachment observed. Rhegmatogenous retinal detachment was also observed in 4 eyes after the removal of silicone oil, etinal detachment in 3 more eyes was

observed in the late postoperative period (between 3 and 24 months) in the eyes without endotamponade. In total, 28 (5.8%) of the operated eyes had a postoperative retinal detachment of rhegmatogenous origin. Logistic regression analysis found that complete adhesion of the posterior hyaloid increased the risk of recurrent detachment by approximately 10 times. Tractional-rhegmatogenous detachment of the retina as an indication for surgery was found to increase the risk of postoperative detachment by 26 times, and tractional retinal detachment by 21 times (compared to vitreous hemorrhage). Among the intraoperative factors, severe hemorrhage observed during membrane dissection (by 14 times) and iatrogenic tears (16 times) were found to increase risk of recurrent retinal detachment.

Twenty-four of the 28 eyes were operated on for recurrent retinal detachment. In 20 eyes (71.4%) retinal attachment was obtained after repeated surgery. Rhegmatogenous retinal detachment was observed in 7 eyes at the last examination, and phthisis bulbi was observed in 1 eye after repeated operations.

Retinal vascular occlusive complications in the postoperative period were observed in 5 of 502 eyes (433 patients) which underwent pars plana vitrectomy due to various complications of diabetic retinopathy. These complications included central retina artery occlusion in 4 eyes (0.8%) and central retinal vein occlusion in 1 eye (0.2%).

Chapter X. Results of 25 gauge pars plan vitrectomy for complications of diabetic retinopathy. Results of surgery in 90 eyes (90 patients) which underwent 23 gauge vitrectomy and 31 eyes (31 patients) which underwent 25 gauge vitrectomy for various complications of proliferative diabetic retinopathy in the department of diabetic eye disease of National Ophthalmology Centre named after Academician Zarifa Aliyeva, in 2014-2015, were compared. The patients were observed for at least 6 months after surgery. Combined operations (phacoemulsification, IOL implantation and vitrectomy) were performed in 29 out of 90 eyes in 23 gauge groups (32.2%) and in 11 out of 31 eyes (35.5%) in 25 gauge groups. In general, combined surgery was performed in 36.7% of the phakic eyes in 23 gauge group and in 40.1% of eyes in 25 gauge group ($p = 0.739$).

In both groups, gas tamponade was applied to approximately half of the eyes at the end of the surgery. In 42 out of 90 eyes in 23 gauge group (46.7%), and in 15 out of 31 eyes (48.4%) in 25 gauge group, the vitreous cavity was restored with gas. Sterile air was applied to 22 eyes (24.4%) in 23 gauge group and to 9 eyes (29.0%) in 25 gauge group. Silicone oil (1000 cst) was used in 24 eyes (26.7%) in 23 gauge group and 7 eyes (22.6%) in 25 gauge group. In addition, in 23 gauge vitrectomy group, in 2 eyes (2.2%) at the end of the surgery, the vitreous cavity was restored with BSS solution.

Six months after surgery, visual acuity improved in both groups (LogMAR visual acuity changed from 1.63 ± 0.74 to 0.81 ± 0.36 in 23 gauge group, and from 0.68 ± 0.35 to 1.78 ± 0.80 in 25 gauge group). No statistically significant difference was found between the two groups ($p = 0.085$).

There was no statistically significant difference in the frequency of intraoperative tears between groups. In 23 gauge group, iatrogenic tears were reported in 11 out of 90 eyes (12.2%), and in 25 gauge vitrectomy group, in 5 out of 31 cases (16.1%) ($p > 0.05$). There was no significant difference in the frequency of intraoperative bleeding between groups ($p = 0.245$). The need for a sclerotomy at the end of the surgery was studied among the groups. Only 8 (25.8%) of the 31 eyes in the 25 gauge group required at least 1 suture at the end of the surgery. At least 1 suture was placed at the end of the surgery in 41 (45.6%) of 90 eyes in 23 gauge group ($p = 0.041$). In 23 gauge group, hypotension (intraocular pressure <= 5 mm Hg) was observed in 3 eyes (3.3%) on the 1st day after surgery, and intraocular hemorrhage was observed in 2 of these eyes. In the postoperative period, early vitreous hemorrhage was observed in 13 (14.4%) in 23 gauge group and in 3 eyes (9.7%) in 25 gauge group. During the follow-up period, recurrent hemorrhage was observed in 9 eyes (10.0%) in 23 gauge group and in 2 eyes (6.5%) in 25 gauge group (in both cases $p > 0.05$ between groups). Other complications included 3 rhegmatogenous detachment in 23 gauge group (the retina successfully reattached after surgery). In 25 gauge group, silicone oil penetrated under the conjunctiva in 1 eye.

CONCLUSIONS:

1. Improvements in diagnostic techniques for retinal diseases, increased effectiveness of surgical treatment, reduced risk of surgery have contributed to the expansion of indications for vitrectomy for complications of diabetic retinopathy and the possibility of surgery at an earlier stage. The widespread use of laser and anti-VEGF treatments and the earlier detection of vitreomacular interface changes have led to a reduction in the relative weight of hemorrhagic complications in vitrectomy indications, with a shift to tractional changes, and in many cases overlapping of several indications for vitrectomy [4,8,11,12,13,15,17,27,30,31,33].
2. Mini-invasive (23 gauge and 25 gauge) vitrectomy allows to obtain stable anatomical and functional outcomes both in the early and long term period after surgery for the complications of diabetic retinopathy. In the observations of 6 months or more after the surgery, retina was attached in 98.6% of the eyes, and visual acuity improvement was noted in 85.9%. Vitrectomy for intraocular hemorrhages showed the highest improvement in visual acuity - 96.7% of eyes, macula-off tractional retinal detachment - the lowest - 65.7% of eyes [5,6,9,25,26,28].
3. Both the combined surgery (phacoemulsification and 23 gauge vitrectomy) and vitrectomy alone for the complications of diabetic retinopathy allow to obtain similar long-term functional results. As anterior segment complications are more common in combined surgery, it is advisable to perform the surgery selectively and to closely monitor the eyes for fibrinous uveitis and hypertension in the early postoperative period [1,2,3,16,18].
4. Peeling of the internal limiting membrane membrane during vitrectomy due to complications of diabetic retinopathy increases the anatomical success rate of the surgery and reduces the number of repeated operations. Microperimetry examination revealed that peeling of the internal limiting membrane did not adversely affect retinal sensitivity. OCT examination revealed an asymmetric change in the thickness of the central retina

(thickening of the nasal retina, thinning of the temporal retina) after peeling of the internal limiting membrane.

5. In patients with diabetic retinopathy, intravitreal administration of anti-VEGF agents before vitrectomy may help to reduce intraoperative complications (severe bleeding) and to reduce the frequency of recurrent vitreous hemorrhage in the early postoperative period. This effect helps to accelerate the visual rehabilitation of patients and achieve higher functional results earlier. However, in the long term, the effect of anti-VEGF agents is reduced and does not significantly affect late-onset vitreous cavity hemorrhage and functional outcomes [24,33].
6. Silicone oil provides higher anatomical results in the cases of complex retinal detachments and other serious complications associated with diabetic retinopathy by providing long-term tamponade. Improvement or stabilization of vision in the majority of eyes suggests that the use of silicone oil as a tamponade is effective in severe complications of diabetic retinopathy. Silicone oil-related glaucoma is one of the most serious postoperative complications and a cause of low functional outcomes [7,14,20,21,32].
7. Early and late vitreous cavity hemorrhage after vitrectomy for diabetic retinopathy have different mechanisms. Preoperative intravitreal anti-VEGF injection reduces the risk of early vitreous cavity hemorrhage by 3 times ($p = 0.039$). Preoperative neovascularization in the iris has been found to increase the risk of late vitreous cavity hemorrhage by 9 times ($p < 0.001$). A history of severe cardiovascular or cerebrovascular problems is an important risk factor for both early and late hemorrhages. Observations 1 year or more after mini-invasive vitrectomy in patients with diabetic retinopathy showed that the main types of postoperative glaucoma were silicone oil-related glaucoma (10.8%), neovascular glaucoma (3.6%), and open-angle glaucoma (3.6%). In 81.4% of cases, intraocular pressure was controlled by hypotensive drops, and in 8.6% Ahmed glaucoma valve was implanted. After mini-invasive vitrectomy for complications of diabetic retinopathy, recurrent rhegmatogenous

retinal detachment was observed in 5.8%, occlusive vascular diseases of the retina in 0.9% [7,10,22,23,29].

8. Both 23 gauge and 25 gauge technologies allow to obtain satisfactory results in various complications of diabetic retinopathy. 25 gauge technology can be successfully used in complex retinal pathologies, including tractional and tractional-rhegmatogenous retinal detachments, along with vitreous hemorrhage. Sutureless surgery rate is higher with 25 gauge vitrectomy without silicone oil tamponade than in 23 gauge vitrectomy, which can help increase patient comfort in the early postoperative period. Early postoperative hypotension in sutureless cases was also a distinguishing sign of 23 gauge vitrectomy. All the above-mentioned allows us to predict that in the future, as the technical parameters of vitrectomy devices improve and the arsenal of tools expands, 25 gauge surgery will be more widely used in various complications of diabetic retinopathy [19].

PRACTICAL RECOMMENDATIONS:

1. In the eyes with diabetic retinopathy, if the **vitreous / subhyaloid space hemorrhage** is new, it is recommended to wait 4 weeks and if there is no positive dynamics, to plan a vitrectomy surgery. However, if the other eye is not functional, the surgery may be performed earlier. If a retinal detachment on B-scan or neovascularization of the iris are detected, surgery should be performed immediately. The absence of panretinal laser photocoagulation and the only functioning eye status also are key factors for performing the surgery earlier. Preoperative anti-VEGF is recommended 1 week before surgery in the eyes with iris neovascularization, if there is no detachment on B-scan and the systemic risk is low.

2. In the eyes with diabetic **tractional retinal detachment**, if the fovea-off detachment is new, urgent vitrectomy is recommended. Observation is recommended for fovea-on detachments. However, if there is neovascularization of the iris along with fovea-on detachment, hemorrhage in the vitreous, or tractional edema of the macula, a planned vitrectomy is recommended. Old macular detachments can be treated with a planned vitrectomy (with low functional prognosis). If epiretinal membrane is noted along with tractional detachment, limited ILM peeling is recommended. If there is no intraoperative tear, air or SF_6 tamponade is recommended. In eyes with an intraoperative tears, subretinal fluid drainage and C_3F_8 or silicone oil tamponade are recommended.

3. **Tractional-rhegmatogenous retinal detachment** requires urgent vitrectomy and drainage of subretinal fluid. C_3F_8 tamponade is recommended for upper tears, and silicone oil tamponade for lower tears or significant residual subretinal fluid.

4. In **tractional diabetic macular edema**, if the structure of the outer layers of the retina is damaged non-significantly and the perifoveal perfusion is maintained on OCT, FA and OCT-A examination, vitrectomy and ILM peeling are recommended. Observation is recommended in case of ischemic maculopathy, IS/OS disorganization. In non-tractional edema, selective vitrectomy

and ILM peeling may be performed if anti-VEGF and steroid injections are ineffective and panretinal laser photocoagulation is performed. Low functional prognosis should be discussed with the patient. Vitrectomy and ILM peeling and C_3F_8 tamponade in diabetic **full-thickness macular hole**s, vitrectomy and ILM peeling for lamellar holes with concomitant edma and intact IS / OS, observation if edema is absent, are recommended.

5. In the eyes with **preretinal hemorrhage** with attached posterior hyaloid, planned vitrectomy and air / BSS are recommended. If an intraoperative tear is found, SF_6 tamponade is recommended for upper tears and C_3F_8 tamponade for lower tears.

6. In the cases of **progressive fibrovascular proliferation**, if complete panretinal laser photocoagulation is performed and the systemic risk is low, intravitreal anti-VEGF injection and vitrectomy and limited ILM peeling after 1 week are recommended.

7. In the **phakic** eyes, if there is a concomitant cataract or if the patient is over 50 years of age, combined or two-step surgery (first phacoemulsification and IOL implantation, then vitrectomy) is recommended. The lens can be spared in young patients. Phacoemulsification of cataracts and IOL implantation are recommended during silicone oil removal in eyes with silicone tamponade.

8. In the absence of **preoperative and intraoperative (iatrogenic) tears** partial air or BSS restoration of the vitreous cavity is recommended at the end of vitrectomy for complications of diabetic retinopathy. If a tear is found, SF_6 for the upper tears, C_3F_8 or silicone oil tamponade for the lower tears (especially in the cases of residual subretinal fluid, taking into account the patient's ability to lie down in a forced position and the status of the only functioning eye) are recommended.

LIST OF SCIENTIFIC PUBLICATIONS ON THE SUBJECT OF THE DISSERTATION:

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LIST OF ABBREVIATIONS:

DM – diabetes mellitus
DME– diabetic macular edema
DR – diabetic retinopathy
DRVS – Diabetic Retinopathy Vitrectomy Study
ILM – internal limiting membrane
IOP - intraocular pressure
OCT - Optical coherence tomography
SRF – subretinal fluid
VEGF - vascular endothelial growth factor

The defense will be held on 22 June 2022 at 14^{00} at the meeting of the Dissertation council BED 1.03 of Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at Academician Zarifa Aliyeva National Ophthalmology Centre.

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Abstract was sent to the required addresses on 20 May 2022.