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Modern approaches to the surgical treatment of large full-thickness macular holes

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Abstract

Vitreoretinal surgery is an actively developing area of modern ophthalmic surgery. Intravitreal interventions in the central retina with large full-thickness macular holes deserve special attention. This article provides an overview of the scientific literature published in journals recommended by the Higher Attestation Commission, also presented in the scientific databases Scopus, PubMed, dedicated to modern techniques to the surgical treatment of large full-thickness macular holes. The main methods for closing defects in the macular area today are the use of various modifications of the inverted internal limiting membrane flap technique and the application of autologous platelet rich plasma in a macular hole. These techniques provide high anatomical and functional outcomes. Modifications of the inverted internal limiting membrane flap technique demonstrated effectiveness in such complex clinical situations as recurrent macular holes, concomitant high myopia, retinal detachment. Over the past 10 years, data on the use of autologous platelet-rich plasma for this group of patients appeared in the scientific literature. More accurate surgical procedures are required for the use of this technique compared with the standard methods, but this technique is applicable in all patients, does not require additional manipulations (blood sampling and centrifugation), additional equipment. Vitreoretinal interventions with the use of platelet-rich plasma are characterized by relative simplicity and ease of carrying out surgical procedures. However, it is important to consider the possibility of pseudouveitis development, the need for additional equipment. Since both of these methods demonstrate good anatomical results, the problem of choosing a technique in a particular clinical case remains. It was clear that the method of surgical intervention should be chosen, taking into account possible disadvantages and limitations to the method, as well as the skills of an ophthalmic surgeon. The lack of a unified approach to macular hole surgery encourages researchers to improve surgical techniques, develop and implement new modifications of surgical approaches.

Keywords: macular holes**,** inverted internal limiting membrane flap technique, displaced internal limiting membrane flap, Platelet-rich plasma, PRP, Autologous Conditioned Plasma, ACP.

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Over the past 10 years, vitreoretinal surgery has undergone significant changes in terms of surgical equipment, instrument, and technique improvements [1]. Moreover, the diagnostic capabilities to detect vitreoretinal pathology have been improved [2]. These improvements were also implemented in the field of vitreomacular interface pathology, particularly in large-diameter complete macular holes (CMH). However, despite the active development of endovitreal interventions for CMH, unresolved issues and certain problems in choosing the surgical intervention method remained [2].

This study aimed to summarize and compare the treatment methods for CMH to identify their advantages and disadvantages.

The treatment of CMH is surgical. Small-diameter MH can spontaneously close; therefore, they require case follow-up or minimal surgical intervention. As a rule, vitrectomy without internal limiting membrane (ILM) peeling is sufficient, and using chemical (pharmacological) vitreolysis, the pneumovitreolysis is possible [3–5]. CMH of a larger diameter does not show a tendency to regress. On the contrary, with increased existence

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duration, the diameter of the defect increases [6].

Nowadays, the most widely used surgical intervention method for CMH includes a 3-port *pars plana* vitrectomy with retinal ILM peeling, postoperative vitreal cavity tamponade using a gas-air mixture or sterile air, and subsequent positioning of the patient "face down" for 1 day or more [7]. The performed endointervention provides good anatomical and functional results but is not always effective in large-diameter CMH [8]. Therefore, new surgical intervention techniques are being developed, and the existing ones are being improved.

The retinal ILM removal during endovitreal intervention for CMH is one of the most delicate manipulations in vitreoretinal surgery. The first report in the medical literature on ILM peeling in MH surgery was published in 1997 by Eckardt et al. [9]. In their study, the vitreosurgeon performed a complete mechanical ILM removal around the macular defect. Researchers reported successful closure of MHs in 92% of cases. Data on good anatomical and functional results were also confirmed by the findings of other ophthalmic surgeons [10, 11]. However, information in the literature does not offer good results on ILM removal around the defect in the surgical treatment of large-diameter MH [12], which prompted researchers for further macular surgery research.

In 2010, Z. Michalewska et al. reported on the ILM inverted valve method for large-diameter MH treatment. The researchers suggested maintaining the ILM area adhesion around the foveolar defect, followed by overlapping the formed flap into the hole on both sides [13]. This method has demonstrated encouraging results in MH surgery, and the authors noted MH closure in 98% of cases,(with an average minimum diameter of the MH of 698 μm) [13].

Over the past decade, the results of interventions using this technique have been published in the literature, confirming its efficiency [14, 15]. However, overlapping of the ILM flap causes certain difficulties, especially at the time of replacing the fluid with air, as the ILM remnants accumulate around the MH. Thus, various modifications of the ILM inverted valve method began to appear [16–22].

Since the end of the XX century, after the method of treating MH using ILM peeling was first used, data have accumulated in macular surgery on both the positive and negative aspects of using this method. A good anatomical result is indisputable when using ILM peeling, especially when using various modifications of the ILM inverted valve method, namely, the anatomical closure is achieved in 98%–100% of cases [23–25], and MH relapses do not occur [26]. With long-term MHs, peeling was also proven to be more effective [27].

The negative consequences of ILM peeling include injury to Müller cells according to retinal electron microscopy data, slow and incomplete recovery according to electroretinography data [28], and dissociation of the retinal nerve fiber layer [29]. In the postoperative period, some patients have visual field defects, more often on the nasal side [30]; however, some researchers attribute these changes, not to ILM peeling, but gas-liquid exchange during vitrectomy [31].

Various modifications of the ILM inverted valve method have been proven effective in such difficult clinical situations as recurrent MH, concomitant high-grade myopia, and retinal detachment [17–19, 32].

Methods for performing surgical intervention in macular surgery are being improved, and various adjuvants have recently been introduced, the most common is platelet-rich plasma (PRP) and autologous conditioned plasma.

PRP is plasma obtained from autologous human blood with a platelet concentration of up to $1000 \times \times 10^9$/l [33]. The first reports on the possibility of using PRP in MH surgery appeared in the international literature at the end of the XX century. Since then, numerous modifications have appeared [34, 35]. Several researchers believe that ILM peeling is required before PRP application [36–39], while others suggest performing surgery without the ILM peeling [40, 41]. Vitrectomy without peeling with an enzyme (collagenase) solution application before applying PRP to the MH zone is also reported [42].

The use of PRP application has demonstrated its efficiency in large-diameter CMH surgery, as anatomical closure of the MH is achieved in 86%–100% of cases [36, 38]. The use of PRP in surgery for CMH is associated with high myopia [43] and repeated surgical interventions for MH [44, 45]. This method is characterized by the relative simplicity of the surgical procedures. However, the use of PRP has several aspects, such as the need for equipment for blood centrifugation and increased financial costs for surgical intervention [46].

The process of obtaining PRP requires rather "rigid" centrifugation, which can destroy platelets and worsen the properties of the obtained material [47]. Preoperatively, the patient's blood should be taken into a syringe, the blood should be centrifuged in a special tube, and the resulting PRP is collected. Notably, the system turns out to be "open" during these actions, which is associated with possible contamination of the completed PRP [47]. The literature provides reports about the development of a pseudo-uveal reaction in the anterior chamber and vitreous cavity [48].

In recent years, publications on this subject have increasingly described the use of autologous conditioned plasma in vitreoretinal, including macular surgery [48–51]. Autologous conditioned plasma, compared to PRP, is characterized by a higher degree of purification of the resulting platelet-rich plasma from other blood elements, particularly leukocytes [47]. When using the autologous conditioned plasma, the biomaterial is directly taken into a specially designed double syringe [48], which is centrifuged. PRP is injected into the internal syringe, which reduces the risk of infection of biological material. Extremely low leukocyte count reduces the risk of pseudo-uveal reaction [48].

Thus, to date, the method of the inverted valve of the ILM in various modifications and the application of PRP in the MH are most actively used in large-diameter CMH surgery. These methods demonstrate high anatomical and functional efficiency. When using modified ILM inverted valve methods, more sparing surgical procedures are required compared to traditional methods of surgical intervention; however, this applies to all patients, which does not require additional manipulations (blood sampling and centrifugation) or additional equipment. The use of PRP applications is characterized by the simplicity and convenience of performing surgical procedures. However, the risk of developing a pseudo-uveal reaction, as well as the need for additional equipment, should be considered.

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