

# Management of Malignant Glaucoma

Reza Sadeghi<sup>1</sup>, Ali Momeni<sup>1</sup>, Ghasem Fakhraie<sup>1</sup>, Yadollah Eslami<sup>1</sup>, Reza Zarei<sup>1</sup>, Zakieh Vahedian<sup>1</sup>, Mona Safizadeh<sup>1</sup>, Seyed Mehdi Tabatabaei<sup>1</sup>

<sup>1</sup>Glaucoma Service, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran

## Abstract

**Purpose:** To compare the outcomes of various invasive and noninvasive approaches to the treatment of malignant glaucoma.

**Methods:** Glaucoma-related keywords were looked up in PubMed and Google Scholar, and related articles up to 2022 were used to put together this review article.

**Results:** Numerous surgical methods and techniques have been introduced in the past few years. This review outlined current knowledge regarding the nonsurgical and surgical management of malignant glaucoma. In this regard, we first briefly outlined the clinical presentation, pathophysiology, and diagnosis of this disorder. Then, the current evidence on the management of malignant glaucoma was reviewed. Finally, we discuss the need for treatment of the other eye and the factors that might affect the outcome of surgical intervention.

**Conclusions:** Fluid misdirection syndrome, or malignant glaucoma, is a severe disorder that can occur spontaneously due to surgical intervention. The pathophysiology of malignant glaucoma is complicated, and numerous theories exist about the underlying mechanisms that may contribute to the disease. Malignant glaucoma can be treated conservatively using medications, laser therapy, or surgery. Laser treatments and medical treatments have been adequate for the treatment of glaucoma, but the effects have generally been short-lived, and surgical treatment has proved to be the most effective. There have been a variety of surgical methods and techniques introduced. Still, none have been studied in a large proportion of patients as a control case to compare effectiveness, outcomes, and recurrence. Pars plana vitrectomy with irido-zonulo-capsulectomy still seems to have the best results.

**Keywords:** Fluid misdirection syndrome, Laser therapy, Malignant glaucoma, Medical intervention, Surgical intervention

**Address for correspondence:** Seyed Mehdi Tabatabaei, Farabi Eye Hospital, Qazvin Square, Tehran, Iran.

E-mail: meh.tabatabaei@gmail.com

**Submitted:** 09-May-2022; **Revised:** 03-Sep-2022; **Accepted:** 14-Sep-2022; **Published:** 29-Apr-2023

## INTRODUCTION

Fluid misdirection syndrome is a severe complication that can happen during or after anterior segment surgery.<sup>1</sup> It is extremely difficult to treat, and the prognosis for long-term stabilization of intraocular pressure (IOP) is often dubious. Inadequate uniform clinical case clarification impairs our understanding of pathogenesis, risk factors, proper diagnosis, and appropriate treatment. Prior classifications for this syndrome were imprecise and lacked a broad perspective. In addition, this syndrome has been called different names, some emphasizing the presumed pathophysiology, including infusion misdirection syndrome, acute intraoperative rock-hard eye syndrome, ciliary

block, subcapsular fluid entrapment, malignant glaucoma, and positive vitreous pressure glaucoma. Years after von Graefe's first description in 1869, we now understand much more about malignant glaucoma, yet its management remains inconclusive.

Perimeter glaucoma occurs in between 2% and 4% of patients who have had penetration surgery for acute or chronic angle-closure glaucoma. In a recent study, malignant glaucoma happened in 1.3% of all eyes following surgery, which included 1689 nonpenetrating and penetrating surgeries conducted as glaucoma surgery alone or in combination with cataract surgery.<sup>2</sup> This problem occurred in 2.3% of eyes following penetrating surgery, substantially more common than

### Access this article online

Quick Response Code:



**Website:**  
www.jcurrophthalmol.org

**DOI:**  
10.4103/joco.joco\_147\_22

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Sadeghi R, Momeni A, Fakhraie G, Eslami Y, Zarei R, Vahedian Z, *et al.* Management of malignant glaucoma. *J Curr Ophthalmol* 2022;34:389-97.

nonpenetrating surgery. It also occurs after different types of surgeries, including laser iridotomy,<sup>3</sup> glaucoma drainage device implantation,<sup>4</sup> phacoemulsification<sup>5</sup> posterior capsulotomy with Nd: YAG laser (Neodymium-yttrium-aluminum-garnet laser),<sup>6</sup> cyclophotocoagulation,<sup>7</sup> large-sized intraocular lens implantation,<sup>8</sup> local miotics application,<sup>9</sup> suture lysis after trabeculectomy,<sup>10</sup> and even spontaneously.<sup>11</sup> Malignant glaucoma has been reported in eyes when glaucoma had not previously been diagnosed. It is more common in eyes affected by angle closure glaucoma. It was more frequently reported in females, which may be related to the smaller anterior part of the eyeball in these patients.<sup>12</sup> This problem can occur at various time points following the operation, sometimes immediately and sometimes later.

This review outlines current knowledge regarding the surgical and medical management of malignant glaucoma. We first briefly outline the clinical presentation, pathophysiology, and diagnosis of this syndrome. After that, we look in more depth at the current evidence about how to treat malignant glaucoma.

## METHODS

For this review, PubMed and Google Scholar were searched for related keywords, such as fluid misdirection syndrome, malignant glaucoma, surgical management, laser therapy, and medical management, and relevant articles from 2000 to 2022 were selected. Furthermore, the search results were confined to human studies. After the initial search, the first screening of articles was done by a rapid review of article topics. Selected papers underwent a second screening by reviewing their abstracts. As this manuscript is a review article, taking informed consent was not relevant.

## RESULTS

Using the keywords and related MeSHs, we found six review articles, seven retrospective studies articles, 28 case reports, 12 case series, and a systematic review and case series; we also found two letters and two reports and used them for this article.

## DISCUSSION

Malignant glaucoma presents as uniform shallowness of the anterior chamber in association with a high or even normal IOP and a patent peripheral iridotomy. The lack of pupillary block must be established by the existence of a patent iridotomy, and posterior segment disease (especially suprachoroidal hemorrhage) must be ruled out by a meticulous fundus examination. The initial sign is frequently an enhancement in near vision as a result of forward displacement of the lens iris diaphragm. It can be difficult to identify early in the course of malignant glaucoma before IOP increase develops. Although the IOP is normally greater than 21 mmHg in the majority of eyes, it may be normal or low in some cases.<sup>13</sup> When the IOP increases spontaneously, pain and inflammation occur, and corneal edema may develop. Ultrasound biomicroscopy (UBM)

of the eyes during a malignant glaucoma episode reveals anterior rotation of the ciliary processes that press against the lens equator and limit the normal flow through the anterior chamber.<sup>1,13,14</sup> Malignant glaucoma may be part of a spectrum caused by a modest idiopathic supraciliary effusion that contributes to anterior rotation of the ciliary body, fluid misdirection, and anterior segment structural displacement.<sup>1</sup>

Malignant glaucoma might also occur in aphakic, phakic, or pseudophakic eyes. Aphakic malignant glaucoma is the emergence of symptoms following cataract surgery or the persistence of symptoms following cataract extraction for phakic malignant glaucoma.<sup>15</sup>

The origins of malignant glaucoma are not completely understood. There are numerous ideas on the elements that could help it progress. There is little assurance about the biochemical processes or structures that contribute to the progression of malignant glaucoma, and its etiology appears to be complex. It has been postulated that anterior rotation of the ciliary body processes results in ciliolenticular contact and ciliary obstruction.<sup>16</sup> The main structural hallmark of malignant glaucoma is the forward displacement of a relatively large lens, which therefore restricts communication between the posterior and anterior chambers.<sup>16</sup> Uveal tract congestion may contribute to the lens being pushed forward. In addition, the lens capsule and zonules may act as a barrier to the passage of aqueous humor into the anterior chamber.<sup>16</sup>

Inflammation or miotics-induced swelling of the ciliary processes might result in a crucial constriction of the anatomically small space between the ciliary body and the lens equator, resulting in a relative obstruction of forwarding aqueous flow.<sup>9</sup> Furthermore, abnormal choroidal circulation might result in blood buildup and enlargement of the ciliary processes. Epstein *et al.* postulated that malignant glaucoma results from a diminished permeability of the anterior hyaloid or vitreous body to the anterior passage of aqueous humor into the anterior chamber.<sup>17</sup> There are probably some eyes that are predisposed to malignant glaucoma due to connective tissue pathology caused by a preponderance of intercellular material composed primarily of glycosaminoglycans. Glycosaminoglycans generated by abnormal connective tissue fibroblasts aggregate in the vitreous of malignant glaucoma eyes.<sup>1</sup> Glycosaminoglycans, in conjunction with proteins accumulated in the vitreous body as a result of decreased transscleral outflow, contribute to the rise in oncotic pressure and water accumulation. In addition, the increased viscosity induced by the mucopolysaccharides complicates the fluid flow from the posterior to the anterior chamber. Moreover, glycosaminoglycans might potentially cause injury to the iridocorneal angle.<sup>1</sup>

The co-occurrence of anatomical and physiological susceptibilities, as well as alterations in IOP of the anterior chamber after surgery, activates a unique pump mechanism induced by lens-iris diaphragm motions, which might affect the progression of malignant glaucoma. This malignant

mechanism can take on a variety of forms, with clinical manifestations starting immediately following surgery when stimulating variables cannot be balanced in the eyeball's closed system (acute malignant glaucoma).<sup>18</sup> On the other hand, if a relative equilibrium is achieved between the volume of generated fluid and the outflow from the eyeball, malignant glaucoma symptoms may be delayed (chronic malignant glaucoma).

Pupillary block glaucoma must be considered in patients who have a high IOP and a shallow anterior chamber. The existence of a patent iridotomy or iridectomy helps to rule out this entity. In contrast to malignant glaucoma, which causes uniform anterior chamber shallowing, pupillary block glaucoma is characterized by an iris bombe and a shallow-to-flat peripheral anterior chamber but a reasonable depth in the central anterior chamber. A second iridotomy using an Nd: YAG laser should be done if the patency of an iridotomy is in doubt. Choroidal detachments are prevalent following glaucoma filtration operations and might be mistaken for malignant glaucoma due to the anterior chamber depth being shallow or flat. Eyes with choroidal detachments are often hypotonic. IOP readings may be inaccurate in some circumstances when the anterior chamber is flat, making the differentiation between the two conditions problematic. Xu *et al.* showed that the lens, the anterior vitreous, and the ciliary body all play a role in the pathophysiology of malignant glaucoma.<sup>19</sup> Multiple blocking variables may occur simultaneously or sequentially as the disease advances. Removal of blockers is necessary for successful therapy. Ciliary edema and inflammation can lead to ciliary separation and lower IOP when IOP is too high. It is imperative to have surgery as soon as possible to reestablish the anterior chamber and address the ciliolenticular block. With zonulo-hyaloido-vitreotomy in the treatment of malignant glaucoma, vision can be improved in the vast majority of cases.<sup>20</sup> The treatment for malignant glaucoma can be successful. Naderi Beni *et al.* demonstrated that pseudophakic malignant glaucoma patients had a high success rate with peripheral irido-capsulo-hyaloidotomy using laser or surgical technique in the inferior quadrant. Pseudophakic malignant glaucoma patients were treated primarily by establishing a patent inferior connection between the vitreous cavity and anterior chamber.<sup>21</sup> Xiong and Kim describe a case of bilateral angle closure with increased IOPs that appear to be rather common in nature. Anterior displacement of the intraocular lens, axial shallowing, increasing IOP, and a myopic shift in the left eye were all observed following cataract surgery. In addition to resolving the angle closure, the procedure also restored normal IOP and corrected the patient's myopia.<sup>22</sup> Sarrafpour *et al.* showed that a 40-year-old woman with developmental delays and a history of self-abuse was found to have malignant glaucoma with an anterior chamber traumatic cataract. Anesthesia and a UBM revealed that the lens had slipped into the anterior chamber. The posterior pressure was eased by preemptive pars plana vitrectomy (PPV), and the anterior chamber was reformed by

irido-zonulo-hyaloido-vitreotomy (IZHV). A clear corneal incision was possible because of these maneuvers.<sup>23</sup> Patients with chronic open-angle glaucoma who choose minimally invasive glaucoma surgery hope to avoid or postpone the need for invasive glaucoma surgery. By increasing drainage beneath the conjunctiva, XEN45 reduces IOP. Marzo *et al.* presented data on a patient who developed malignant glaucoma after phacoemulsification, IOP insertion, and XEN45 implant. While effective, it is not immune to major adverse effects in some circumstances.<sup>24</sup> A rare delayed consequence of cataract surgery is the development of malignant glaucoma. A growing tendency toward myopia can be an indicator of this process early on. While IOP is frequently uncontrollable without surgery, as in the presented example, it is also treatable with less invasive methods. Therefore, it is important to tailor treatment to the specifics of each case and carefully consider whether or not a vitrectomy is indeed essential.<sup>25</sup> Malignant glaucoma is particularly challenging to handle consequences after ocular surgery. Although it can occur on its own or after any ocular procedure, glaucoma surgery is where it is most commonly seen. When an axial stromal flattening occurs alongside a patent peripheral iridotomy, a clinical diagnosis can be made. Sometimes, even with a rise, IOP might be considered normal. Even though its precise cause is uncertain, numerous suggested pathways have been explored.

Choroidal effusions are often pale brown elevations that dissolve on their own. Ultrasonography should be used if the view of the fundus is obstructed. Suprachoroidal hemorrhage, which typically arises hours or days following intraocular surgery and is frequently heralded by hypotony, must also be ruled out by clinical examination and ultrasound examination. Typically, the symptoms are sudden onset, excruciating throbbing eye pain. Typically, these eyes have more inflammation than those with serous choroidal detachments. Moreover, choroidal elevations are clinically evident when the anterior chamber is flat and the IOP is elevated; ultrasound examination reveals dome-shaped elevated choroidal detachments with little or no movement on dynamic B-scan. Furthermore, in each patient following a glaucoma filtration operation, the likelihood of a wound leak or over-filtration must be ruled out as a possible cause of a shallow or flat anterior chamber through meticulous examination. Both of these diseases will result in an IOP that is normal to low.

Malignant glaucoma may benefit from irido-zonulo-hyaloidotomy and PPV, two surgical procedures that reduce IOP and enhance visual outcomes in Chew *et al.*'s study. On the way in, an 81-year-old woman complained of throbbing pain in her right eye, blurred vision, and a red eye. The right-eye visual acuity was 6/60. Slightly shallow anterior chamber and grade 0 gonioscopy by Shaffer's grading (edematous cornea). A 52 mmHg IOP was recorded. The optic disc is pink with a cup-disc ratio of 0.3. Despite medication, laser treatment, and the Chandler operation, IOP was not satisfactorily controlled; therefore, a complete PPV was performed. Without the use of medication, IOP was maintained in the mid-teens postoperatively.<sup>20</sup> Six

out of nine people reported an improvement in their vision. Irido-zonulo-hyaloidotomy with complete PPV minimizes the risk of future relapses by making the decision early on.<sup>20</sup> Research by Pathak Ray *et al.* reported ostial IZHV which was intraoperatively performed on 11 primary angle closure glaucoma patients. Postoperative aqueous misdirection was not observed in any of the patients. It is possible to use ostial IZHV to avoid postoperative aqueous misdirection in glaucoma patients with high-risk features. An anterior segment surgeon can do ostial IZHV, minimizing the need for a vitreoretinal surgeon.<sup>26</sup>

Malignant glaucoma is more prone to developing in the eyes with greater resistance to vitreous fluid flow. Vitreous in its natural state does not obstruct the free route of water, and its fluid conduction decreases as the pressure difference increases. When the transvitreous flow is inadequate to balance the pressure difference between the vitreous and anterior chambers, compression of the vitreous increases. This reduces the fluid conductivity. The surface via which aqueous escapes the vitreous is constrained by the ciliary body's circle and the vitreous's central apposition to the lens, resulting in a doughnut-shaped zone. Vitreous compression along with anterior movement gradually reduces the diffusional area. Additionally, hyperopic eyes with a shorter axial length and a proportionally larger lens would have a doughnut-shaped zone that is half the size of normal-sized eyes.<sup>27</sup> According to Tomey *et al.*, postoperative wound leakage during cataract surgery might be an important factor in the development of malignant glaucoma. The initial forward displacement of the iris-lens diaphragm generated by the wound leak appears to initiate a cycle of aqueous misdirection and accumulation in the posterior section. This may be exacerbated in some cases by the lack of iridectomy. Remarkably, filtration operation with enhanced aqueous outflow could also be a cause.<sup>28</sup>

The goal of medical treatment is to decrease aqueous humor production and vitreous shrinkage while concurrently reducing resistance in the channel of aqueous humor flow into the anterior chamber. Several medical treatments have been used with different mechanisms of action. Mydriatics and cycloplegics work through paralysis of the ciliary muscle, ciliary ring widening, zonule apparatus tightening, and backward movement of the lens. Moreover, osmotically active agents are helpful via increasing the blood osmolality, causing water molecule movement from the eyeball towards hyperosmotic plasma, which leads to a reduction of the vitreous body hydration and makes it feasible to retract the iris-lens diaphragm and extend the anterior chamber. In addition, beta-blockers suppress the production of aqueous humor. Carbonic anhydrase inhibitors reduce the aqueous humor secretion by suppressing carbonic anhydrase activity within the epithelium of the ciliary body. Corticosteroids limit inflammatory edema in the region of the ciliary. In contrast to pupillary block, this condition does not respond to miotics. Miotics are not appropriate for the management of malignant

glaucoma because they cause relaxation of the zonules and make the lens move forward.<sup>15</sup>

Nonetheless, the efficacy of these treatments varies between different studies. According to published data, around 50% of patients respond to medicinal therapy. However, in the study of Debrouwere *et al.*, the number of patients with malignant glaucoma who recurred following conservative treatment was equivalent to 100%, despite an initially favorable response to such therapy. In addition, conservative treatment fails to reverse the pathogenic process in the vast majority of patients with malignant glaucoma.<sup>29</sup> Even if such treatment achieves IOP control, long-term cycloplegia is required to sustain this effect in many eyes.<sup>16</sup> When drugs are discontinued or modified, it has been reported that malignant glaucoma symptoms tend to reappear. As a result, medical treatment is considered to be temporary and is utilized in conjunction with laser iridotomy, posterior capsulotomy, and hyaloidotomy. The current acceptable conservative treatment regimen includes the application of atropine, phenylephrine, blockers, and acetazolamide locally, as well as the administration of 50 percent glycerol solution in oral dosages and mannitol intravenously. Local corticosteroids have the effect of reducing the associated inflammatory process. If improvement is obtained, the dose of hyperosmotic can be reduced, followed by carbonic anhydrase inhibitors. Nonetheless, mydriatic-cycloplegic medications should be continued.<sup>1</sup>

In phakic and pseudophakic eyes, Nd:YAG laser iridotomy combined with anterior hyaloidotomy and posterior capsulotomy has been shown to stabilize IOP.<sup>30</sup> This method results in the release of any water trapped inside the vitreous. After the anterior hyaloid face rupture, ultrasound biomicroscopic imaging demonstrated normalization of anterior rotation of the ciliary body and shallowing of the anterior chamber.<sup>31</sup> The technique, however, may have a short-term effect with a relapse rate of 75%, likely because the basic misdirection mechanism is not counteracted, allowing fresh aqueous to collect in the vitreous cavity. Additionally, restricting the aqueous flow among the zonules or between the lens capsule and ciliary processes may cause an inflammatory response, particularly in eyes with residual cortical lens material.<sup>5</sup> The efficiency of transscleral cyclophotocoagulation has been emphasized by several studies.<sup>32,33</sup> The ciliary-hyaloid interface is disrupted by coagulative necrosis and shrinking of the ciliary processes. Along with reducing aqueous production, this interruption might permit normal aqueous flow and posterior mechanical rotation of the ciliary body. This treatment should be investigated; however, other ophthalmologists prefer a nondestructive approach, particularly in patients with acceptable vision. Notably, this method does not exacerbate the complexity of subsequent surgical procedures.

Surgical intervention may be essential in several instances. Certain authors emphasize the importance of expeditious surgical treatment for long-term success. In addition, eyes with a higher IOP and a shorter axial length may have a

worse prognosis. Surgical intervention instead can be used when different treatment methods or laser treatment are not successful. The treatment's primary premise is that the removal of vitreous and aqueous humor from the vitreous cavity and the development of interaction with the anterior chamber assists in interrupting the vicious cycle that ultimately results in augmented IOP. PPV reduces aqueous collection within the vitreous cavity. It has been described as the preferred treatment for pseudophakic malignant glaucoma. According to some studies, an entire vitrectomy, rather than a partial vitrectomy, is preferable.<sup>34</sup> This, however, may not be enough to break the cycle of malignant glaucoma because it is hypothesized that all tissues, including the iris, lens capsule, zonule, and anterior vitreous, must be removed to establish a permanent route between the vitreous cavity and anterior chamber.<sup>32,35,36</sup>

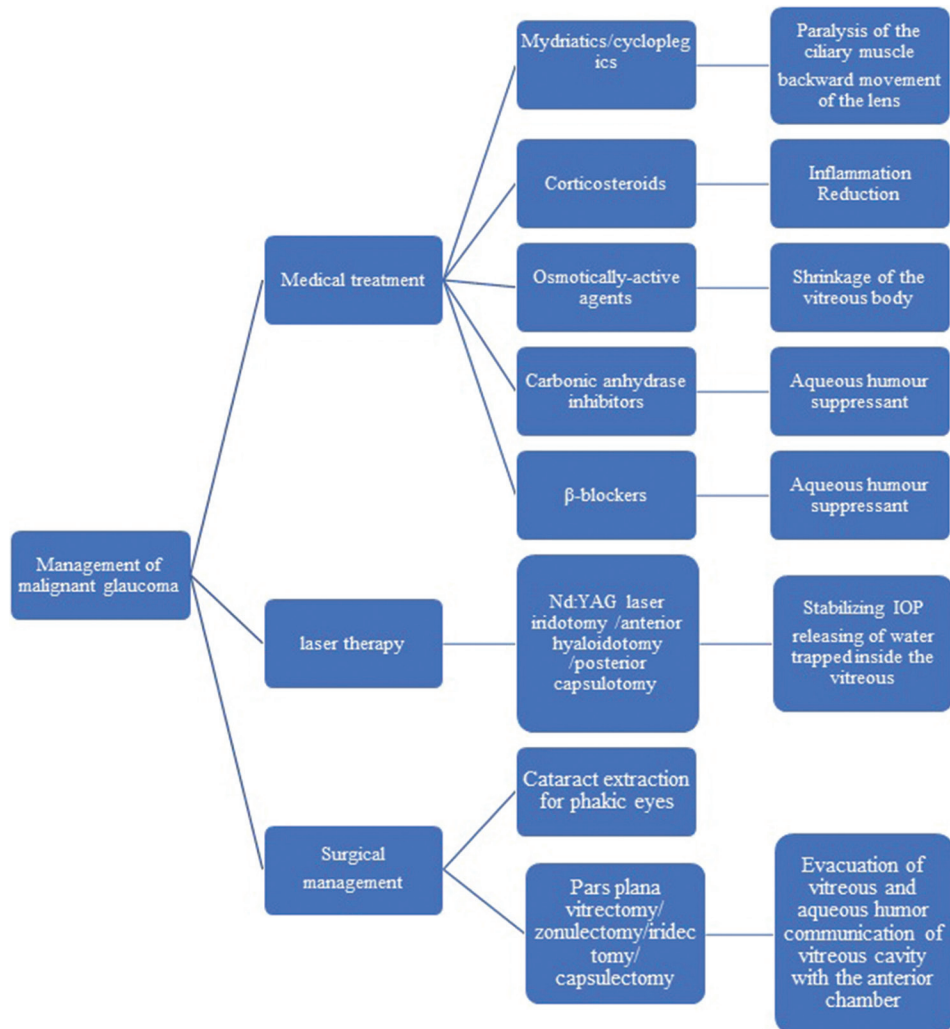
In addition, Debrouwere *et al.* stated that total vitrectomy was ineffective in 66% of their patients if zonulectomy was not performed concurrently as a part of treatment. The peripheral vitreous can seldom be entirely removed with standard vitrectomy, which contributes to the high relapse rate. Only total vitrectomy in conjunction with zonulectomy, iridectomy, and capsulectomy has been shown to result in relatively complete success in large groups of patients.<sup>29,35</sup> It is critical to preserve the patency of newly formed passways with an Nd:YAG laser throughout surgical follow-up. Zonulo-hyaloido-vitrectomy has been offered as an alternative surgical treatment for pseudophakic malignant glaucoma by anterior segment surgeons.<sup>37-39</sup> In this operation, the anterior vitrectomy is performed through a tunnel within the iridectomy. The surgery has been stressed as being safer because the iridectomy is performed in full visual sight, as opposed to a blind approach through the pars plana. Although the first findings of such a surgery are favorable, relapse may occur in up to 40% of patients. This is because the channel is blocked by vitreous or fibrin.<sup>39</sup> A recent study in Saudi Arabia demonstrated the efficacy of vitrectomy in conjunction with hyaloido-capsulo-iridectomy in a group of 69 eyes. With surgical microscope illumination, a two-port PPV can be as effective as a three-port treatment.<sup>40</sup> Several studies have found that removing the anterior hyaloid face through capsulectomy, rather than debulking the vitreous, is the most important factor in treating fluid misdirection syndrome.<sup>41-43</sup> Small-gauge procedures may be just as effective as conventional 20-gauge vitrectomy.<sup>42</sup> The majority of instances mentioned in the literature involve pseudophakic eyes. When malignant glaucoma develops in a phakic eye, most investigations recommend doing a vitrectomy and cataract extraction simultaneously.<sup>36,43</sup> Harbour *et al.* emphasize the importance of lensectomy in eyes with significant dense cataracts, corneal edema, or when the anterior chamber does not deepen sufficiently following vitrectomy.<sup>44</sup> Tsai *et al.* found a superior surgical outcome with the inclusion of a posterior capsulectomy.<sup>43</sup> For the best results, Sharma *et al.* suggest performing a vitrectomy first, then phacoemulsification, and finally a secondary vitrectomy and zonulo-hyaloidectomy to

relieve posterior pressure.<sup>36</sup> According to Chaudhry *et al.*, preventative PPV during contralateral cataract surgery may be useful if one eye has aqueous misdirection after surgery.<sup>45</sup> The many approaches to treating malignant glaucoma are summarized in Figure 1.

Numerous surgical procedures have been suggested to correct malignant glaucoma in phakic and pseudophakic eyes. Studies that talk about vitrectomy with hyaloido-zonulo-iridectomy make a difference between vitrectomy done through the pars plana and into the posterior chamber and vitrectomy through the anterior chamber.

The posterior technique involves performing an anterior, core, partial, or complete vitrectomy, followed by making the hyaloido-zonula-iridectomy from behind using the vitrector. Debrouwere *et al.* evaluated an anterior PPV alone, an anterior PPV in combination with hyaloido-zonula-iridectomy, and a complete PPV in combination with hyaloido-zonula-iridectomy. They found a reoccurrence rate of 75% in pseudophakic patients treated with a PPV alone and a reoccurrence rate of 66% in pseudophakic patients treated with an anterior PPV plus hyaloido-zonula-iridectomy.<sup>29</sup> None of the 15 patients treated with a combination of PPV and hyaloido-zonula-iridectomy relapsed. The study had a short follow-up interval of 10, 24, and 61 days for PPV, anterior PPV with hyaloido-zonula-iridectomy, and complete PPV with hyaloido-zonula-iridectomy, respectively. Subsequent research has validated the low recurrence rate associated with complete PPV with hyaloido-zonula-iridectomy.<sup>36,40,46,47</sup> Relapse rates varied in studies that used anterior, core, or partial PPV with hyaloido-zonula-iridectomy.<sup>48,49</sup> One study documented a recurrence that was cured with slit-lamp needling on a single eye.<sup>50</sup> However, it should be noted that certain studies do not define the type of vitrectomy performed on the pars plana.<sup>32,51</sup> When the anterior route is chosen, the hyaloido-zonula-iridectomy is performed from the anterior chamber, followed by an anterior vitrectomy via the hyaloido-zonula-iridectomy. Numerous studies have demonstrated that this technique has a low relapse rate.<sup>52,53</sup> However, one study found that four out of ten eyes relapsed.<sup>54</sup>

Obstruction of the passage between the posterior and anterior chambers may cause malignant glaucoma to reappear following full vitrectomy with hyaloido-zonula-iridectomy. Mardelli reported a pseudophakic patient with malignant glaucoma that was treated with anterior PPV and hyaloido-zonula-iridectomy but relapsed a few days following surgery.<sup>50</sup> Slit-lamp needling established direct connectivity between the anterior chamber and the vitreous cavity, which resolved the problem, and a block of blood and vitreous was suspected of causing the relapse.<sup>50</sup> Dave *et al.* presented four patients with pseudophakia with malignant glaucoma treated with PPV and hyaloido-zonula-iridectomy who all relapsed due to an inflammatory membrane or the haptic of an intraocular lens preventing the iridectomy or hyaloidotomy. Laser



**Figure 1:** The management of malignant glaucoma

membranotomy or laser hyaloidotomy was used to treat all patients successfully.<sup>54</sup> Balaggan and Laidlaw used anterior PPV, phacoemulsification, and irido-capsulo-hyaloidectomy to successfully treat a patient and create a path through the lens capsule.<sup>55</sup> The necessity of direct contact between the vitreous cavity and the anterior chamber, which is ensured by the hyaloido-zonula-iridectomy, is highlighted in these examples.

Compared to vitrectomy from the anterior chamber, PPV with hyaloido-zonula-iridectomy allows the surgeon to remove the vitreous more thoroughly. One could argue that disrupting the anterior hyaloid face, as well as the zonules and iris, is the most crucial phase. Still, fluid may continue to fill the vitreous's remaining cisterns, forcing the iris forward. Vitrectomy using the anterior method has the advantage of sparing the conjunctiva and being performed by an anterior segment surgeon. However, moving in a narrow anterior chamber may be challenging, posing a risk of corneal endothelial injury. With the anterior technique, it may be more difficult to remove all of the hyaloid that could restrict the passage through the iridectomy. It is also hard to verify that the anterior hyaloid is

disturbed because the vitreous can shift backward because of the anterior chamber water flow.

Patients who have one eye with malignant glaucoma are at augmented risk of developing the same issue in the other.<sup>56,57</sup> Prophylactic procedures such as discontinuing miotic drops, prescribing atropine, or performing a prophylactic vitrectomy should be explored before surgery.<sup>15</sup> It has been advised that patients at risk of malignant glaucoma would benefit from combined phacoemulsification and a core vitrectomy through an anterior approach, as well as an iridotomy or iridectomy if cataract surgery is necessary due to chronic angle closure.<sup>57</sup> However, if one eye gets malignant glaucoma after surgery, preventive procedures such as vitrectomy with hyaloido-zonula-iridectomy may be looked into if the other eye also needs surgery.

Up to now, procedures have been described to treat malignant glaucoma after it occurs and has required the expertise of a vitreoretinal surgeon, though IZHV has recently been described in the treatment of pseudophakic malignant glaucoma.<sup>37</sup>

Notwithstanding, surgeons face an impasse when persistent anterior chamber shallowing occurs intraoperatively during phacotrabeculectomy in the absence of supra-choroidal hemorrhage, despite intense cycloplegia and tight suturing on the operating table. Most likely, the aqueous fluid in these eyes was moved during surgery, and they are at a high risk of getting malignant glaucoma after surgery. Tang *et al.* showed that it was accomplished through intraoperative procedures such as gonioscopy and zonula removal (with or without the periphery of the capsular bag) that allowed us to ensure that we removed as much of the vitreous as possible, thus confirming our success in the surgery, as well as enhancing our ability to see through the iris. There was also less stress to the conjunctiva due to the 23G vitrector, which allowed for faster wound healing than with previous methods.<sup>58</sup>

Pathak Ray *et al.* described a simple method for anterior vitrectomy through the ostium in previously unreported cases of combined phacotrabeculectomy, which can help prevent this serious complication in at-risk patients. All complications in this cohort were directly related to the filtration procedure, and during the postoperative period, none of the eyes developed malignant glaucoma. Their findings suggest that ostial IZHV may be considered for postoperative prevention of malignant glaucoma in a subgroup of glaucoma patients with high-risk characteristics.<sup>26</sup> The anterior segment surgeon is capable of successfully performing ostial IZHV, thereby reducing the patient's reliance on a vitreoretinal surgeon. However, there is scarce evidence regarding the prevention of postoperative malignant glaucoma. This could be a promising area of future research.

If malignant glaucoma continues to be a challenging clinical problem, it will result in irreversible blindness if not treated promptly and adequately. The surgeon must be aware of at-risk eyes preoperatively and closely monitor them during follow-up appointments. Early detection is critical for preventing irreparable visual loss. The prognosis is highly variable and is determined by the duration and severity of the malignant glaucoma event. In patients with early-stage glaucoma, if the attack is halted and IOP is effectively controlled, the prognosis can be favorable. The issue is that malignant glaucoma frequently resists conventional therapy, and laser techniques are not always beneficial. In such circumstances, partial PPV combined with capsulotomy connecting the vitreous cavity and the anterior chamber is an effective technique of intervention in terms of IOP management, postoperative corrected distance visual acuity, and medication reduction. The prognosis following laser and surgical treatment is dependent on the occurrence of complications. Complications following malignant glaucoma surgery include increased IOP during the early postoperative period; inflammatory effusion; hyphema; the occurrence of posterior adhesions; and lack of efficacy of filtration surgery before the onset of malignant glaucoma, macular edema, and retinal detachment.<sup>59</sup> In the case of postoperative anterior chamber shallowing, it is feasible to do a capsulotomy using iridectomy, and in most situations, the use of an Nd:YAG laser is a safe and successful procedure.

In a recent study, Thompson *et al.* investigated the factors that affect the surgical outcome of malignant glaucoma. They reported that vitrectomy was more likely to be successful in patients with a history of 3 incisional surgeries, IOP 30 mmHg, or 3 glaucoma drops. They also observed that if vitrectomy was performed within 30 days, recovery of anatomy, best visual acuity, and IOP occurred sooner. IOP reduction was greater in subjects treated with oral carbonic anhydrase inhibitors or Nd:YAG laser hyaloidotomy and without a history of malignant glaucoma.<sup>60</sup>

Malignant glaucoma is an uncommon but dangerous complication. Although medical and laser modalities contribute to the management of malignant glaucoma, their effects are mostly temporary. Thus, the main effective modalities of treatment are surgical interventions. Numerous surgical methods and techniques have been introduced in the past few years. However, no large-scale controlled study has investigated the efficacy, outcomes, and reoccurrence of these modalities. Almost all previous studies are case series of patients with small sample size, and there is no controlled clinical trial in this regard. However, it seems that a complete PPV combined with irido-zonulo-capsulectomy to eradicate the pressure difference between the chambers would achieve the best results.

#### **Financial support and sponsorship**

Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

## **REFERENCES**

1. Foreman-Larkin J, Netland PA, Salim S. Clinical Management of Malignant Glaucoma. *J Ophthalmol.* 2015;2015:283707. doi:10.1155/2015/283707.
2. Krix-Jachym K, Żarnowski T, Rekas M. Risk Factors of Malignant Glaucoma Occurrence after Glaucoma Surgery. *J Ophthalmol.* 2017;2017:9616738. doi:10.1155/2017/9616738.
3. Cashwell LF, Martin TJ. Malignant glaucoma after laser iridotomy. *Ophthalmology.* 1992;99(5):651-658; discussion 658-659. doi:10.1016/s0161-6420(92)31913-x.
4. Greenfield DS, Tello C, Budenz DL, Liebmann JM, Ritch R. Aqueous misdirection after glaucoma drainage device implantation. *Ophthalmology.* 1999;106(5):1035-1040. doi:10.1016/S0161-6420(99)00530-8.
5. Lynch MG, Brown RH, Michels RG, Pollack IP, Stark WJ. Surgical vitrectomy for pseudophakic malignant glaucoma. *Am J Ophthalmol.* 1986;102(2):149-153. doi:10.1016/0002-9394(86)90135-2.
6. Mastropasqua L, Ciancaglini M, Carpineto P, Lobefalo L, Gallenga PE. Aqueous misdirection syndrome: a complication of neodymium: YAG posterior capsulotomy. *J Cataract Refract Surg.* 1994;20(5):563-565. doi:10.1016/s0886-3350(13)80238-6.
7. Azuara-Blanco A, Dua HS. Malignant glaucoma after diode laser cyclophotocoagulation. *Am J Ophthalmol.* 1999;127(4):467-469. doi:10.1016/s0002-9394(98)00359-6.
8. Reed JE, Thomas JV, Lytle RA, Simmons RJ. Malignant glaucoma induced by an intraocular lens. *Ophthalmic Surg.* 1990;21(3):177-180.
9. Rieser JC, Schwartz B. Miotic-induced malignant glaucoma. *Arch Ophthalmol Chic Ill 1960.* 1972;87(6):706-712. doi:10.1001/archophth.1972.01000020708018.
10. DiSclafani M, Liebmann JM, Ritch R. Malignant glaucoma following

- argon laser release of scleral flap sutures after trabeculectomy. *Am J Ophthalmol.* 1989;108(5):597-598. doi:10.1016/0002-9394(89)90441-8.
11. González-Martín-Moro J, Iglesias-Ussel L, Cobo-Soriano R, Fernández-Miguel Y, Contreras I. Spontaneous malignant glaucoma: Case report and review of the literature. *Saudi J Ophthalmol Off J Saudi Ophthalmol Soc.* 2019;33(4):398-400. doi:10.1016/j.sjopt.2018.11.005.
  12. Rzehghinejad MR, Amini H, Esfandiari H. Lesser anterior chamber dimensions in women may be a predisposing factor for malignant glaucoma. *Med Hypotheses.* 2005;64(3):572-574. doi:10.1016/j.mehy.2004.07.035.
  13. Trope GE, Pavlin CJ, Bau A, Baumal CR, Foster FS. Malignant glaucoma. Clinical and ultrasound biomicroscopic features. *Ophthalmology.* 1994;101(6):1030-1035. doi:10.1016/s0161-6420(94)31222-x.
  14. Tello C, Chi T, Shepps G, Liebmann J, Ritch R. Ultrasound biomicroscopy in pseudophakic malignant glaucoma. *Ophthalmology.* 1993;100(9):1330-1334. doi:10.1016/s0161-6420(93)31479-x.
  15. Shahid H, Salmon JF. Malignant glaucoma: a review of the modern literature. *J Ophthalmol.* 2012;2012:852659. doi:10.1155/2012/852659.
  16. Ruben S, Tsai J, Hitchings RA. Malignant glaucoma and its management. *Br J Ophthalmol.* 1997;81(2):163-167. doi:10.1136/bjo.81.2.163.
  17. Epstein DL, Hashimoto JM, Anderson PJ, Grant WM. Experimental perfusions through the anterior and vitreous chambers with possible relationships to malignant glaucoma. *Am J Ophthalmol.* 1979;88(6):1078-1086. doi:10.1016/0002-9394(79)90420-3.
  18. Grzybowski A, Prasad S. Acute aqueous misdirection syndrome: Pathophysiology and management. *J Cataract Refract Surg.* 2014;40(12):2167. doi:10.1016/j.jcrs.2014.10.016.
  19. Xu QQ, Wang WW, Zhu J, Liu JR. An unusual case of malignant glaucoma with ciliary detachment. *Int J Ophthalmol.* 2021;14(12):1988-1992. doi:10.18240/ijo.2021.12.27.
  20. Chew RP, Irwan Chong A, Zamli AH, Muhammed J. Successful Management of Malignant Glaucoma With Irido-Zonulo-Hyaloidotomy and Complete Pars Plana Vitrectomy. *Cureus.* 2022;14(1):e21679. doi:10.7759/cureus.21679.
  21. Naderi Beni A, Fesharaki H, Ghanbari H, Kianersi F, Naderi Beni B, Naderi Beni B. Clinical efficacy of inferior peripheral irido-capsulohyaloidotomy for pseudophakic malignant glaucoma. *Int Ophthalmol.* 2021;41(9):3153-3161. doi:10.1007/s10792-021-01880-4.
  22. Xiong AS, Kim DB. Malignant glaucoma presenting with uncontrolled intraocular pressure and myopic refractive surprise after cataract surgery. *Clin Case Rep.* 2022;10(6):e05810. doi:10.1002/ccr3.5810.
  23. Sarrafpour S, Davies I, Ahmed O, Liu J, Teng CC. Cataract Surgery in Malignant Glaucoma from Complete Subluxation of Lens into Anterior Chamber. *J Curr Glaucoma Pract.* 2021;15(3):164-167. doi:10.5005/jp-journals-10078-1320.
  24. Montolio Marzo S, Lanzagorta Aresti A, Davó Cabrera JM, Alfonso Muñoz EA, Piá Ludeña JV, Palacios Pozo E. Malignant glaucoma after XEN45 implant. *Arch Soc Espanola Oftalmol.* 2019;94(3):134-137. doi:10.1016/j.oftal.2018.10.023.
  25. Wiedenmann C, Boneva S, Anton A, Reinhard T, Lübke J. [Chronification of malignant glaucoma after cataract surgery]. *Ophthalmol Z Dtsch Ophthalmol Ges.* 2021;118(2):175-179. doi:10.1007/s00347-020-01088-4.
  26. Pathak Ray V, Gulati I, Choudhari N. Intra-Operative Ostial Irido-Zonulo-Hyaloido-Vitrectomy with Primary Posterior Capsulectomy for Prevention of Post-Operative Aqueous Misdirection in Combined Phaco-Trabeculectomy in Primary Angle Closure Glaucoma. *Curr Eye Res.* 2019;44(10):1087-1090. doi:10.1080/02713683.2019.1625409.
  27. Quigley HA. Angle-closure glaucoma-simpler answers to complex mechanisms: LXVI Edward Jackson Memorial Lecture. *Am J Ophthalmol.* 2009;148(5):657-669.e1. doi:10.1016/j.ajo.2009.08.009.
  28. Tomey KF, Senft SH, Antonios SR, Shammam IV, Shihab ZM, Traverso CE. Aqueous misdirection and flat chamber after posterior chamber implants with and without trabeculectomy. *Arch Ophthalmol Chic Ill 1960.* 1987;105(6):770-773. doi:10.1001/archophth.1987.01060060056032.
  29. Debrouwere V, Stalmans P, Van Calster J, Spileers W, Zeyen T, Stalmans I. Outcomes of different management options for malignant glaucoma: a retrospective study. *Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Clin Exp Ophthalmol.* 2012;250(1):131-141. doi:10.1007/s00417-011-1763-0.
  30. Little BC, Hitchings RA. Pseudophakic malignant glaucoma: Nd:YAG capsulotomy as a primary treatment. *Eye Lond Engl.* 1993;7 ( Pt 1):102-104. doi:10.1038/eye.1993.21.
  31. Grzybowski A, Kanclerz P. Acute and chronic fluid misdirection syndrome: pathophysiology and treatment. *Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Clin Exp Ophthalmol.* 2018;256(1):135-154. doi:10.1007/s00417-017-3837-0.
  32. Dave P, Senthil S, Rao HL, Garudadri CS. Treatment outcomes in malignant glaucoma. *Ophthalmology.* 2013;120(5):984-990. doi:10.1016/j.ophtha.2012.10.024.
  33. Stumpf TH, Austin M, Bloom PA, McNaught A, Morgan JE. Transscleral cyclodiode laser photocoagulation in the treatment of aqueous misdirection syndrome. *Ophthalmology.* 2008;115(11):2058-2061. doi:10.1016/j.ophtha.2008.05.026.
  34. Zhou C, Qian S, Yao J, *et al.* Clinical Analysis of 50 Chinese Patients with Aqueous Misdirection Syndrome: a Retrospective Hospital-based Study. *J Int Med Res.* 2012;40(4):1568-1579. doi:10.1177/147323001204000437.
  35. Rekas M, Krix-Jachym K, Żarnowski T. Evaluation of the Effectiveness of Surgical Treatment of Malignant Glaucoma in Pseudophakic Eyes through Partial PPV with Establishment of Communication between the Anterior Chamber and the Vitreous Cavity. *J Ophthalmol.* 2015;2015:873124. doi:10.1155/2015/873124.
  36. Sharma A, Sii F, Shah P, Kirkby GR. Vitrectomy-phacoemulsification-vitrectomy for the management of aqueous misdirection syndromes in phakic eyes. *Ophthalmology.* 2006;113(11):1968-1973. doi:10.1016/j.ophtha.2006.04.031.
  37. Żarnowski T, Wilkos-Kuc A, Tulidowicz-Bielak M, *et al.* Efficacy and safety of a new surgical method to treat malignant glaucoma in pseudophakia. *Eye Lond Engl.* 2014;28(6):761-764. doi:10.1038/eye.2014.53.
  38. Başgöl Pasaoglu I, Altan C, Bayraktar S, Satana B, Basarır B. Surgical Management of Pseudophakic Malignant Glaucoma via Anterior Segment-Peripheral Iridectomy Capsulo-Hyaloidotomy and Anterior Vitrectomy. *Case Rep Ophthalmol Med.* 2012;2012:794938. doi:10.1155/2012/794938.
  39. Madgula IM, Anand N. Long-term follow-up of zonulo-hyaloido-vitrectomy for pseudophakic malignant glaucoma. *Indian J Ophthalmol.* 2014;62(12):1115-1120. doi:10.4103/0301-4738.149128.
  40. Al Bin Ali GY, Al-Mahmood AM, Khandekar R, Abboud EB, Edward DP, Kozak I. Outcomes of pars plana vitrectomy in the management of refractory aqueous misdirection syndrome. *Retina Phila Pa.* 2017;37(10):1916-1922. doi:10.1097/IAE.0000000000001430.
  41. Byrnes GA, Leen MM, Wong TP, Benson WE. Vitrectomy for ciliary block (malignant) glaucoma. *Ophthalmology.* 1995;102(9):1308-1311. doi:10.1016/s0161-6420(95)30870-6.
  42. Meng L, Wei W, Li Y, Hui X, Han X, Shi X. 25-Gauge pars plana vitrectomy for ciliary block (malignant) glaucoma. *Int Ophthalmol.* 2015;35(4):487-493. doi:10.1007/s10792-014-9974-0.
  43. Tsai JC, Barton KA, Miller MH, Khaw PT, Hitchings RA. Surgical results in malignant glaucoma refractory to medical or laser therapy. *Eye Lond Engl.* 1997;11 ( Pt 5):677-681. doi:10.1038/eye.1997.176.
  44. Harbour JW, Rubsamens PE, Palmberg P. Pars plana vitrectomy in the management of phakic and pseudophakic malignant glaucoma. *Arch Ophthalmol Chic Ill 1960.* 1996;114(9):1073-1078. doi:10.1001/archophth.1996.01100140275003.
  45. Chaudhry NA, Flynn HW, Murray TG, Nicholson D, Palmberg PF. Pars plana vitrectomy during cataract surgery for prevention of aqueous misdirection in high-risk fellow eyes. *Am J Ophthalmol.* 2000;129(3):387-388. doi:10.1016/s0002-9394(99)00405-5.
  46. Hosoda Y, Akagi T, Yoshimura N. Two cases of malignant glaucoma unresolved by pars plana vitrectomy. *Clin Ophthalmol Auckl NZ.* 2014;8:677-679. doi:10.2147/OPHTH.S60704.
  47. Moinul P, Luong M, Bhamra J, Kherani A, McWhae J, Crichton ACS. Aqueous misdirection masked as myopia after cataract surgery. *Can J Ophthalmol J Can Ophtalmol.* 2017;52(4):e146-e148. doi:10.1016/j.cjco.2017.01.022.
  48. Patel S. Pars plana vitrectomy combined with irido-zonulo-hyaloidectomy for aqueous misdirection. *Eur J Ophthalmol.* 2020;30(2):396-398. doi:10.1177/1120672119872056



49. Raj S, Thattaruthody F, Joshi G, Seth NG, Kaushik S, Pandav SS. Treatment outcomes and efficacy of pars plana vitrectomy-hyaloidotomy-zonulectomy-iridotomy in malignant glaucoma. *Eur J Ophthalmol.* 2021;31(1):234-239. doi:10.1177/1120672119877139.
50. Mardelli PG, Mardelli ME. Slit-lamp Needling of the Anterior Capsule for Aqueous Misdirection After Hyaloido-zonulectomy and Iridectomy. *J Glaucoma.* 2018;27(4):e77-e79. doi:10.1097/IJG.0000000000000877.
51. Varma DK, Belovay GW, Tam DY, Ahmed IIK. Malignant glaucoma after cataract surgery. *J Cataract Refract Surg.* 2014;40(11):1843-1849. doi:10.1016/j.jcrs.2014.02.045.
52. Pakravan M, Esfandiari H, Amouhashemi N, Veisi A, Torkian P, Yazdani S. Mini-vitrectomy; a Simple Solution to a Serious Condition. *J Ophthalmic Vis Res.* 2018;13(3):231-235. doi:10.4103/jovr.jovr\_192\_17.
53. Wang J, Du E, Tang J. The treatment of malignant glaucoma in nanophthalmos: a case report. *BMC Ophthalmol.* 2018;18(1):54. doi:10.1186/s12886-018-0714-5.
54. Dave P, Rao A, Senthil S, Choudhari NS. Recurrence of aqueous misdirection following pars plana vitrectomy in pseudophakic eyes. *BMJ Case Rep.* 2015;2015:bcr2014207961. doi:10.1136/bcr-2014-207961.
55. Balaggan KS, Laidlaw DAH. Aqueous misdirection syndrome after pars plana vitrectomy for retinal detachment. *Retin Cases Brief Rep.* 2008;2(1):73-75. doi:10.1097/01.ICB.0000258408.24587.43.
56. Stan C. [Bilateral malignant glaucoma--case report]. *Oftalmol Buchar Rom* 1990. 2005;49(4):33-34.
57. Thompson AC, Challa P. Prophylactic anterior vitrectomy during cataract surgery in eyes at increased risk for aqueous misdirection. *Am J Ophthalmol Case Rep.* 2018;12:24-27. doi:10.1016/j.ajoc.2018.08.002.
58. Tang J, Du E, Li X. Combined Surgical Techniques for the Management of Malignant Glaucoma. *J Ophthalmol.* 2018;2018:9189585. doi:10.1155/2018/9189585.
59. Rekas M, Krix-Jachym K. Malignant glaucoma. *Glaucoma Basic Clin Asp.* Published online 2013:421.
60. Thompson AC, Vu DM, Postel EA, Challa P. Factors impacting outcomes and the time to recovery from malignant glaucoma. *Am J Ophthalmol.* 2020;209:141-150 Basic Clin Asp. Published online 2013:421.