Review Article

Surgical considerations in diabetic vitrectomy

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Abstract: High speed and small gauge vitrectomy systems have made surgical intervention in complications of diabetic retinopathy (DR) safer. The availability of anti-vascular endothelial growth factor (anti-VEGF) compounds for use in DR has significantly improved intraoperative and postoperative outcomes. This review discusses the indications for surgical intervention in DR. The role of anti-VEGF compounds is discussed as surgical adjuvants with an emphasis on timing of treatment before surgery.

Keywords: Vitrectomy; vitreous hemorrhage (VH); diabetic macular edema (DME); taut posterior hyaloid; tractional retinal detachment (TRD); bevacizumab

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Introduction

More than 30 million people in the USA have diabetes (1). It is expected that approximately 25% of these adults (age 20–74 years) with diabetes will develop retinopathy. Diabetic retinopathy (DR) is the primary cause of blindness in this population (1-3). The pathophysiology of DR and its complications is multifactorial and has not been completely elucidated. Although the complications of DR were thought to develop mainly due to microvascular complications of diabetes mellitus, it has now been established that inflammation plays a significant role in the pathogenesis of DR (4-7).

The changes in DR result in progressive retinal ischemia and cellular hypoxia. This process is initiated by a diverse group of pro-angiogenic and inflammatory mediators that initially lead to the development of non-proliferative diabetic retinopathy (NPDR) (8). Following NPDR, as the condition progresses into the advanced phase it leads to proliferative diabetic retinopathy (PDR) with the appearance of new abnormal vessels between the internal limiting membrane (ILM) and posterior hyaloid interface and epiretinal fibrocellular membrane formation (thickened hyaloid). Over time the fibrocellular membranes contract causing traction on the new abnormal vessels. As the hyaloid attachment is now abnormal due to the proliferative nature of the disease and is unable to come away from the retina, the traction from the membranes causes vitreous hemorrhage (VH) and tractional retinal detachment (TRD). If the traction is sufficient to cause a retinal tear, it results in a combined tractional and rhegmatogenous retinal detachment.

Although the management of complications of DR is predominantly surgical, recent progress has been made on treating the condition using anti-VEGF therapy (9).

Indications for pars plana vitrectomy (PPV) in DR

VH

The Diabetic Retinopathy Vitrectomy Study (DRVS)

showed a significant benefit from an early decision to perform vitrectomy surgery on type 1 diabetic patients as delay in surgery leads to further complications and TRD (10). VH remains the most common complication of PDR that causes decreased vision. As vitrectomy systems have become safer and more efficient, the decision to perform surgery for this indication has moved towards earlier intervention (11). Patient input and general health also determines the decision for early surgery. Complications such as a subhyaloid hemorrhage that remains trapped below partially detached vitreous causing significant vision loss is an indication for early intervention. Angle and iris neovascularization and severe PDR in the fellow eye with no previous panretinal laser photocoagulation treatment are also indications for early intervention in these cases.

Postoperative VH following PPV is not uncommon. Some studies report a rate as high as 60% within a few weeks to months after PPV for complications of PDR (12). Fibrovascular tissue growth at sclerotomy sites has been noted as a cause for post PPV associated VH. Gas tamponade, cryopexy to the sclerotomy site, preoperative anti-VEGF treatment and extensive preop PRP have been suggested for preventing postoperative VH in these cases with variable success (13).

TRD

TRD remains a challenging complication for the vitreous surgeon especially if it gets further complicated with a combined tractional and rhegmatogenous retinal detachment. A TRD typically starts over the areas of prominent hyaloid attachment overlying the vascular arcades. Over time, it gradually marches towards the central macula requiring surgical intervention. The TRD may remain peripheral and in these cases when VH does not complicate the clinical situation it can be managed with close observation. Macular heterotopia can result from gradual dragging of the fovea by the proliferation of fibrous tissue. This is another indication to observe macula non-threatening TRD closely as visual outcomes in these cases is poorer (14).

Diabetic macular edema (DME)

DME is the most common cause of vision loss in DR. Approximately 10% of the diabetic population has DME. Surgical intervention for DME is controversial and only indicated in a few limited clinical scenarios. DME secondary to vitreomacular traction (VMT) or taut posterior hyaloid membrane (TPHM) can respond to PPV and removal of traction from the underlying macula. TPHM is identified as a glistening reflex over the macula seen on slit lamp biomicroscopy. On OCT it appears as a hyper reflective membrane with partial posterior vitreous detachment (PVD) and thickened underlying retina. VMT is identified as a partial PVD with focal areas of firm adhesions between the vitreoretinal interface and the retina. Another indication for surgical intervention is the presence of taut ILM with DME unresponsive to treatment post PPV and previously removed posterior hyaloid (15). In the absence of these indications, performing PPV for DME may cause a decrease in vision secondary to progression of cataract, postoperative glaucoma and postoperative VH (16,17). There are reports of improvement of DME in eyes that do not have traction. The mechanism of action of improvement of DME in these cases is unclear. It has been proposed that diabetic eyes have cytokines that promote increased vascular permeability and removal of the vitreous promotes the diffusion of these agents away from the retina. Also, PPV improves oxygenation of the retina which improves the integrity of the blood retinal barrier. The role for PPV in DME other than for the indications discussed remains controversial (18).

Neovascular glaucoma

DR and central retinal vein occlusion remain the most common causes for neovascular glaucoma (NVG). NVG accounts for approximately 5% of blindness in diabetics.

NVG is a complication of advanced and uncontrolled PDR. The pathogenesis is considered to be the effect of vasoproliferative growth factors that arise from widespread retinal ischemia. These diffuse into the anterior segment and cause the growth of new vessels and fibrovascular membranes in the angle thereby obstructing aqueous outflow and causing intraocular pressure (IOP) to rise. There are two aspects of management for this condition. The cause as well as the elevated pressure must be addressed.

Management of this complication is by prompt PRP to the retina. Intravitreal bevacizumab has been used with some success as a short-term solution prior to retinal laser or if PRP fails to cause regression of neovascularization in the anterior segment. Unfortunately, contraction of the fibrovascular membranes in the angle leads to permanently elevated IOP necessitating incisional glaucoma surgical intervention.

In cases with coexistent VH, vitrectomy and endophotocoagulation is the procedure of choice. In these cases, vitrectomy may be combined with endocyclophotocoagulation of ciliary processes to reduce IOP (19). Surgical management of refractory NVG has a higher failure rate than in primary glaucoma due to distorted tissue anatomy and it remains a challenge. Although the concomitant use of anti-VEGF agents is widespread, the long term data on their effectiveness is still inadequate. Trabeculectomy with and without antimetabolites and drainage valves are being increasingly used for the management of this condition with variable success. Cyclodestructive therapy remains an option either as a primary procedure or secondary to failure of primary glaucoma surgical procedures (20).

Cataract surgery in the setting of DR

Cataract surgery in the setting of DR is associated with a higher incidence of postoperative cystoid macular edema as well as worsening of DME (21). The availability of anti-VEGF drug treatment as well as intraocular steroid injections have reduced the incidence of this complication. Prior to the availability of these drugs, the method of choice for treating preoperative DME was focal macular laser treatment to the areas of retinal thickening. Multiple studies have shown the success of bevacizumab, intravitreal triamcinolone acetonide and dexamethasone depot implant. The depot implant has the longest duration of action as it maintains therapeutic levels of drug for a longer duration in the eye. The timing of injection of the drug can be preoperative or intraoperative and gives similar outcomes. Pre and post-surgical OCT scanning of macular thickness are important for monitoring the response of the medication (22,23).

Use of bevacizumab and other drugs as a surgical adjuvant

More recently preoperative use of intravitreal bevacizumab has become accepted as it makes dissection and peeling of fibrovascular membranes in these cases less challenging as well as decreases the incidence of intra and postoperative hemorrhage. Bevacizumab primarily affects blood vessels and causes contraction and vasoconstriction thereby limiting intraoperative hemorrhage. This makes intraoperative maneuvers less challenging due to better visualization. There is a concern for worsening of the detachment caused by contraction of fibrovascular membranes by bevacizumab. A careful preoperative examination is essential for selecting the right case for treatment with anti-VEGF agents (24). Preoperative bevacizumab has a low incidence of TRD development and progression. In a large case series, less than 5% of the cases studied developed or had progression of this complication. It is recommended that intravitreal bevacizumab should be given no more than 2 weeks before surgery as studies have shown that the average number of days for progression or development of TRD was less than 14 days. Studies suggest that the drug should be given within 4 days of surgery as progression and development of TRD occurred 5 days or more after injection in over 80% of cases. Additionally, a higher dose of bevacizumab (2.5 *vs.* 1.5 mg) was associated with a higher chance of TRD development and progression (25).

Conbercept (Langmu; Kanghong Inc., Sichuan, China) is a VEGF receptor (VEGFR) fusion protein. It is a humanized soluble VEGFR protein which comprises extracellular domain 2 of VEGFR-1 and extracellular domains 3 and 4 of VEGFR-2, all of which are combined with the Fc region of human immunoglobulin G1. It functions by competitively inhibiting the binding of VEGF with its receptor by blocking multiple targets, VEGF-A, VEGF-B, and placental insulin-like growth factor. In limited trials it has shown to have benefits similar to bevacizumab by decreasing the incidence of post-operative VH and improving intraoperative visualization (26).

Conclusions

The availability of small gauge high speed vitrectomy systems and the introduction of anti-VEGF and long acting depot steroid medications have contributed significantly to the safe management and successful outcomes in patients with complications of advanced DR. NVG remains a challenge for the ophthalmologists treating this complication. Even though glaucoma valve implant surgeries and anti-VEGF medications are available, the fundamental fact remains that control of the underlying disease is essential for successful outcomes in the diabetic patient.

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