



Diabetic Retinopathy: Surgical Aspects

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5.1 Introduction

Vision loss due to diabetic retinopathy can be devastating and results from numerous complications, including macular edema, retinal and choroidal ischemia, vitreous hemorrhage, tractional retinal detachments, epiretinal membranes (with or without vitreoretinal traction), and papillopathy [1, 2]. The Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) showed that proper blood pressure and blood glucose control can delay the progression of diabetic retinopathy [3–5]. Additionally, local therapies such as focal macular laser, panretinal photocoagulation, intravitreal anti-vascular endothelial growth factor (VEGF), and intravitreal steroids can delay progression of retinopathy and treat associated vision-threatening complications [6]. Nevertheless, some patients continue to progress and require surgical intervention with pars plana vitrectomy (PPV) for optimal vision [6]. An estimated 5% of patients with proliferative diabetic retinopathy required PPV despite laser treatment and good glycemic and hypertensive control in the Early Treatment Diabetic Retinopathy Study (ETDRS) cohort [7].

Traditional indications for surgery include vitreous hemorrhage, macula-involving or macula-threatening tractional retinal detachment, combined tractional and rhegmatogenous

retinal detachment, and diabetic macular edema with or without epiretinal membrane or traction [2, 6].

The goals of diabetic vitrectomy are to clear media opacities such as vitreous hemorrhage, to restore normal retinal anatomy, and to seal any retinal breaks. The latter two goals are accomplished by releasing anterior-posterior and tangential traction on the retina through removal or segmentation of tractional fibrovascular proliferation and epiretinal membranes [2]. The status of the posterior hyaloid is an important factor in the severity of fibrovascular proliferation which can use the adherent vitreous cortex as a scaffold for neovascular expansion. With continued growth, tight tractional membranes form and subsequently contract, promoting vitreous hemorrhage and tractional retinal detachments [8–10]. The removal of the posterior hyaloid face eliminates the scaffolding for subsequent neovascularization, decreasing future tractional forces on the retina. Relief of traction on retinal vessels can also improve blood flow within vessels and reduce leakage [11].

However, even with anatomically successful results after surgery, a patient's vision may ultimately be limited by ischemia from chronic microvascular disease or atrophy secondary to prolonged anatomic abnormalities [12]. Eyes in patients with diabetes typically also have an inherently abnormal vitreoretinal interface which increases the risks of intraoperative bleeding and iatrogenic breaks. Thus, the decision for surgical intervention in this patient population always requires a careful weighing of risks and benefits prior to proceeding.

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5.2 Indications for Surgery

5.2.1 Vitreous Hemorrhage

Vitreous hemorrhage is a common cause of vision loss from proliferative diabetic retinopathy [2]. Hemorrhage can occur from leakage from active neovascularization or traction caused by fibrovascular proliferation on weak vessels (Fig. 5.1). The first successful PPV was performed by

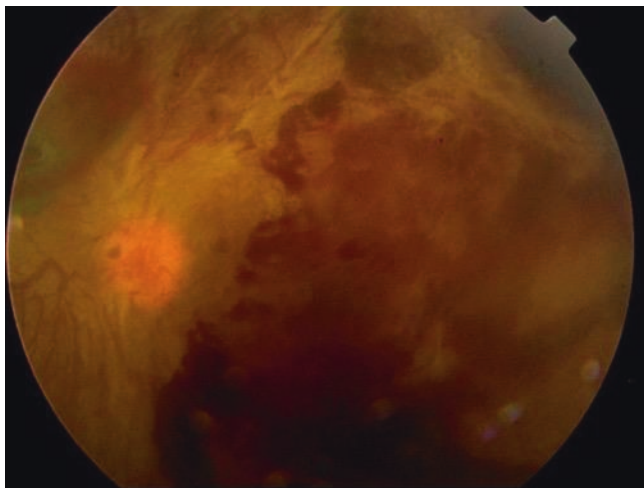


Fig. 5.1 This patient has proliferative diabetic retinopathy with extensive neovascularization radiating from the optic nerve head as well as subhyaloid and vitreous hemorrhage

Machemer in an eye with diabetic vitreous hemorrhage [13]. Historically, ophthalmologists would wait 6–12 months before considering surgery for diabetic vitreous hemorrhage [11]; however, the landmark Diabetic Retinopathy Vitrectomy Study (DRVS) concluded that vitreous hemorrhage in patients with type 1 diabetes benefited from earlier vitrectomy compared to those with type 2 diabetes as these patients tended to develop more aggressive fibrovascular proliferation [14–17]. This study looked at a large cohort of patients with vitreous hemorrhage for at least 1 month and vision 5/200 or worse who were randomized to early vitrectomy within 6 months or observation. The DRVS showed a clear benefit for early surgery in patients with type 1 diabetes, where a delay in surgical intervention more often led to aggressive fibrovascular proliferation and tractional retinal detachment. In this study, 25% of patients undergoing early PPV had a visual acuity of 20/40 or better as opposed to 15% of patients who underwent conventional therapy (observation unless there was a macula-off retinal detachment or NCVH >1 year) [14]. A more recent study showed that at least 87% of patients have an improvement of three lines or greater with a vitrectomy [18].

Commonly, vitreous hemorrhage will settle inferiorly out of the visual axis, or clear spontaneously through the zonules via aqueous outflow. In light of the DRVS results, many clinicians elect to operate after 1 month for type 1 diabetics and 3 months for type 2 diabetics. This, however, is a loose guideline as many other factors are considered prior to surgery: presenting vision, the vision and status of the fellow eye, previous panretinal photocoagulation, history of recurrent vitreous hemorrhage, the patient's daily visual demands, and coexisting conditions such as macula-involving or macula-threatening tractional retinal detachment or ghost cell glaucoma. In the latter scenarios, waiting for surgery may cause irreversible damage. Additionally, earlier surgery

may be warranted for subhyaloid hemorrhage as these hemorrhages tend to be blocked from clearance via the anterior segment. The presence of anterior chamber neovascularization or long-standing vitreous hemorrhage with vitreous base fibrosis blocking the pathway for spontaneous drainage are other indications for early vitrectomy [19].

5.2.2 Tractional Retinal Detachment

Tractional retinal detachments (TRDs) occur from contraction of fibrovascular proliferation on the retina. These detachments tend to be slow growing or stable and can be monitored when they are outside the macula, especially if nasal [20] (Fig. 5.2). One study showed that only 14% of eyes with extramacular TRDs experienced a loss of vision within 1 year [21]. However, for TRDs that involve the macula or for progressively expanding TRDs that are threatening the macula, surgical intervention is usually warranted. A 2008 publication reported that in eyes with a TRD involving the macula, 57% achieved vision of 6/60 or better, whereas in eyes without a macular detachment, 84% could see 6/60 or better [22]. As expected, eyes with a recent history of foveal detachment had a better chance of visual recovery when compared to long-standing ones even if an equally good anatomical result was obtained [23].

Combined tractional and rhegmatogenous retinal detachments occur when the contracting force of the fibrovascular complexes create a retinal break. They can be more convex in configuration and extend further anteriorly [10]. Unlike purely tractional detachments, this kind of detachment can be rapidly progressive and prompt surgery is necessary. These surgeries tend to be complex as separating tightly adherent fibrotic tissue from mobile retina can be difficult and can have worse success rates than detachments without retinal breaks [24]. Despite this, postoperative vision in these patients may improve in up to 70% of eyes [20].

5.2.3 Diabetic Macular Edema

Diabetic macular edema (DME) is the leading cause of visual impairment in patients with diabetes [25, 26]. The role of the vitreous on the development of DME is unclear, but natural history studies have shown that macular edema is more likely to resolve with vitreomacular separation [27, 28]. Eyes with DME more commonly have an attached posterior hyaloid compared to eyes without DME [29]. Diabetic macular edema without clear traction is generally treated with anti-VEGF, intravitreal steroids, and/or focal laser (Fig. 5.3). However, some degree of vitreomacular traction is present in 12% of eyes with DME and up to 24% in eyes undergoing vitrectomy [30]. The subgroup of

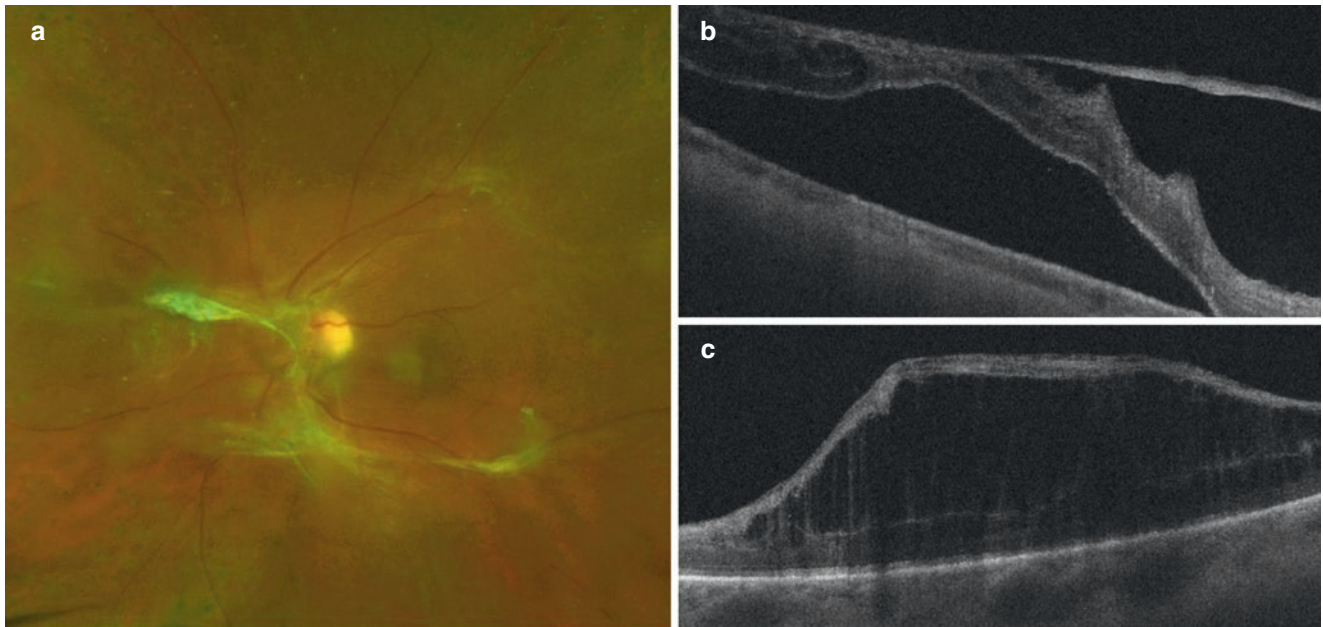


Fig. 5.2 A nasal tractional retinal detachment (**a, b**) and retinoschisis (**a, c**) in a patient with extensive preretinal fibrosis extending from the optic nerve head (**a**). The macula remained well attached without traction, and the patient had a visual acuity of 20/30, so surgery was deferred

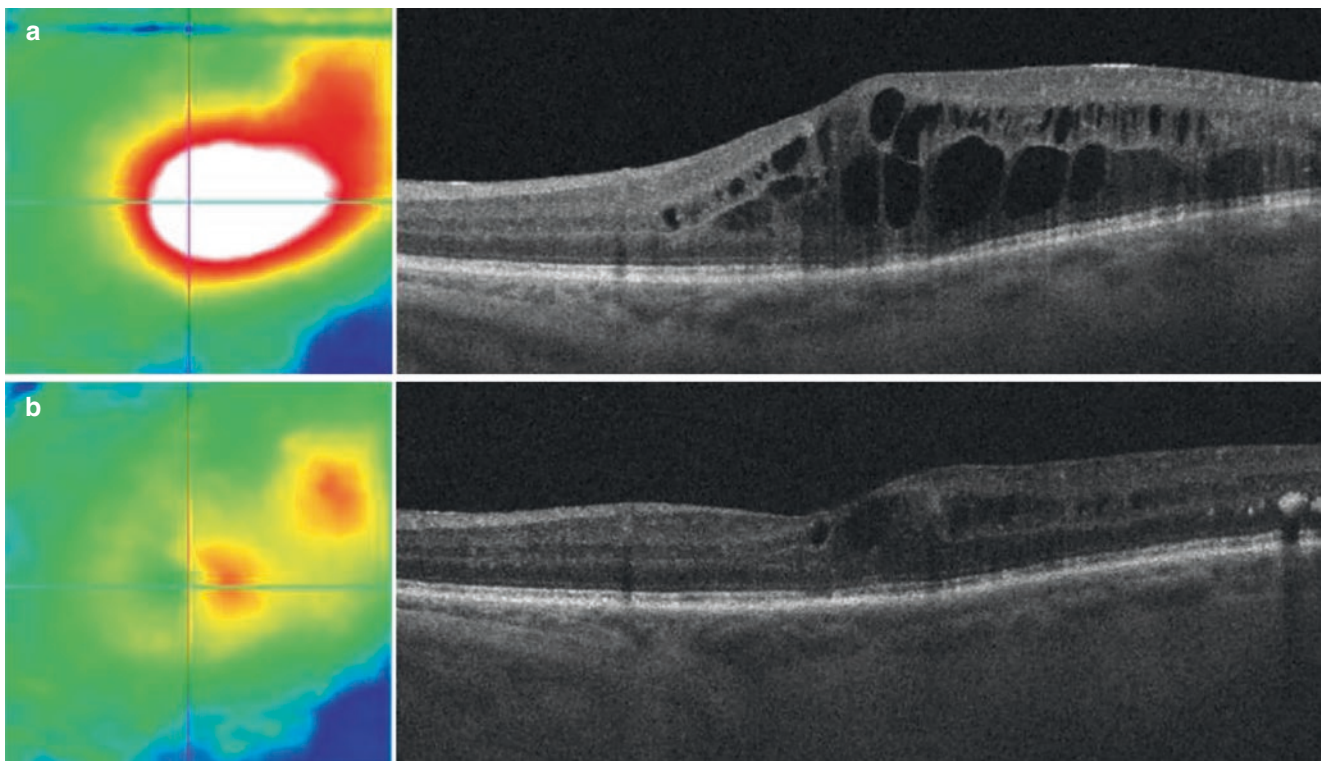


Fig. 5.3 This patient has center-involving diabetic macular edema without an epiretinal membrane (**a**). He underwent serial injections of intravitreal bevacizumab with anatomic and visual improvement (**b**)

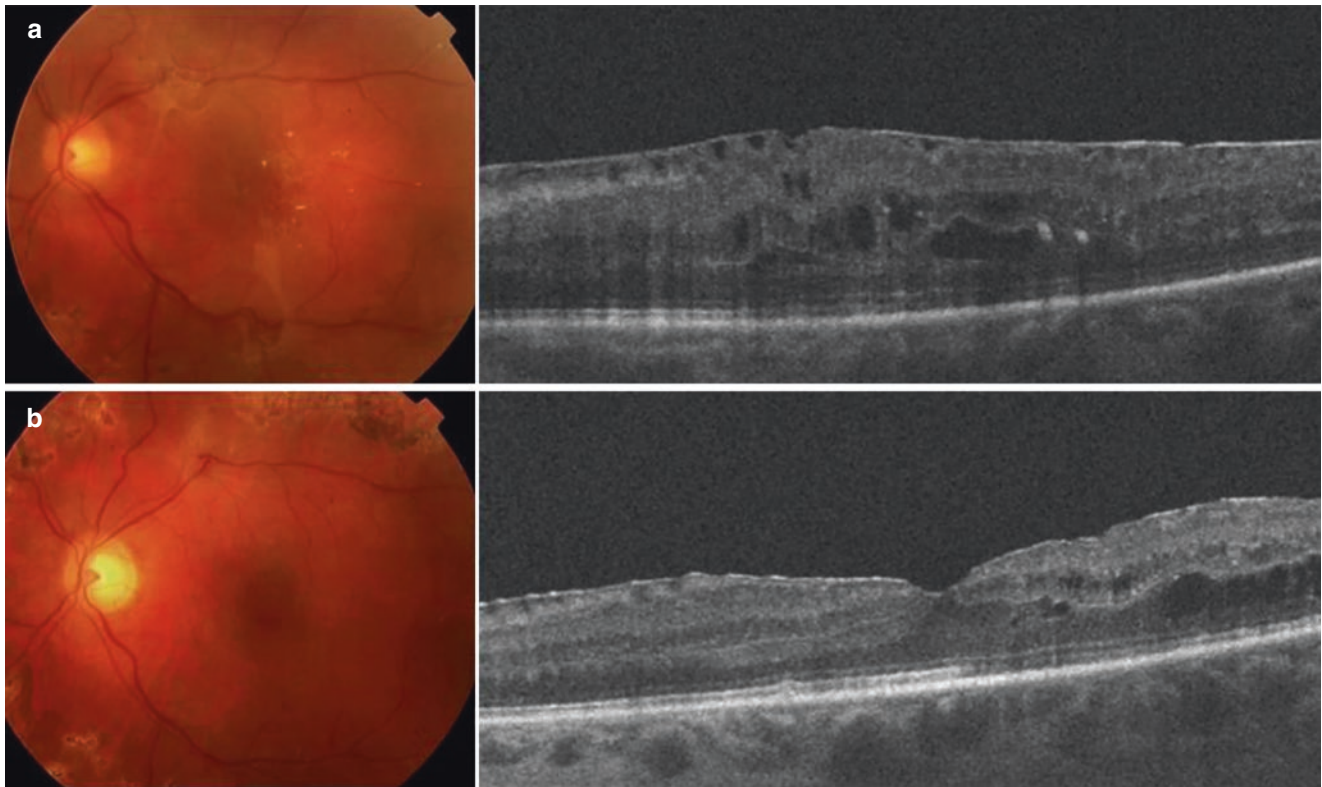


Fig. 5.4 This patient has center-involving diabetic macular edema with an epiretinal membrane (a). Her macular edema was refractory to multiple intravitreal injections of different anti-vascular endothelial growth factor (VEGF) agents, so she underwent vitrectomy with membrane peel.

Subsequently, her vision improved from 20/80 to 20/50 (b). She continues to be treated with intravitreal anti-VEGF to maintain vision but has since developed a recurrent epiretinal membrane

eyes with a taut premacular posterior hyaloid or epiretinal membrane may benefit from vitrectomy [31] (Fig. 5.4). However, even in the absence of clear traction, vitrectomy may be helpful as removal of the vitreous can improve oxygenation and nutrition to the macula and reduce VEGF [32–35]. Vitreous viscosity is 300–2000 times greater than aqueous viscosity [36], which can allow intravitreal molecules such as VEGF to diffuse away from the macula more easily [37, 38]. Similarly, however, intravitreal drugs can also diffuse away from the retina reducing the effective half-life of these medications [39].

The anatomic and functional results of PPV for macular edema appear to vary. In a 2006 randomized controlled trial of PPV with internal limiting membrane (ILM) peeling versus treatment with focal laser, there was no difference in visual or anatomical results between the two treatment modalities [40]. On the other hand, a comparative study of vitrectomy with ILM peeling for diffuse clinically significant macular edema demonstrated structural improvement in foveal thickness and significant improvement in the macular volume but limited visual improvement 12 months

postoperatively [41, 42]. Although not widely performed, the argument for ILM peeling for DME is to relieve tractional forces not visible biomicroscopically from preretinal vitreous or the ILM. As has been shown with previous studies, both functional and anatomic results have varied, with some studies showing benefit of ILM peel [43–47], while others did not [40–42, 48, 49].

A meta-analysis published in 2017 of all randomized clinical trials up to 2014 comparing PPV to focal macular laser or observation showed an improvement of approximately 100 μm in central macular thickness at 6 months for PPV compared to laser or observation; however, that gain was reversed by 12 months [25]. The same meta-analysis showed an insignificant two ETDRS letter vision gain for PPV over laser or observation [25].

Published data comparing macular laser with anti-VEGF treatment, which has become the gold standard for diabetic macular edema, showed an average gain of 6–7 letters at 6–12 months in favor of anti-VEGF therapy. Therefore, PPV does not appear to compare well to anti-VEGF based on historic data; however, it must be recognized that PPV is

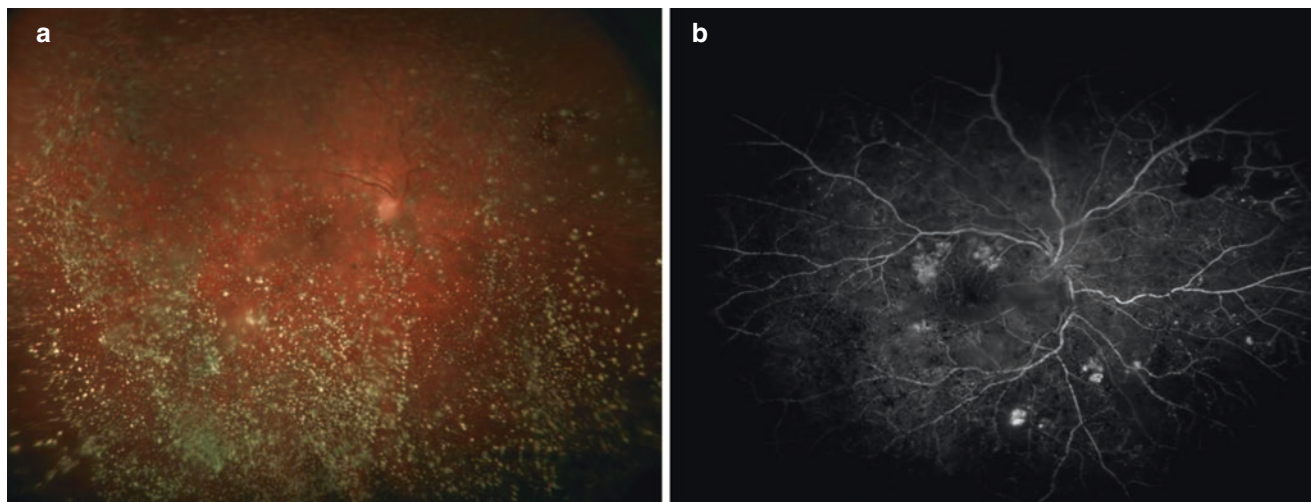


Fig. 5.5 This patient underwent vitrectomy in the right eye for asteroid hyalosis (a) that was limiting the view for retinal examination and adequate placement of in-office panretinal photocoagulation. Preoperative

fluorescein angiography (b) confirmed multiple areas of neovascularization elsewhere

often reserved for patients who are refractive to injections or lasers. Further data comparing PPV with anti-VEGF therapy is needed to directly compare these treatment options.

5.2.4 Miscellaneous

5.2.4.1 Cataract

Patients with diabetes have a higher rate of cataract development than the average population [50]. It is not uncommon for the cataract and/or posterior synechiae from anterior segment neovascularization to limit examination of the retina and/or prevent adequate panretinal photocoagulation. In these situations, cataract surgery is needed. If there is significant posterior neovascularization, the rapid development of a posterior vitreous detachment that can happen with cataract surgery may sometimes lead to vitreous hemorrhage. Additionally, cataract surgery can worsen diabetic retinopathy. The presence of diabetic retinopathy should not be prohibitory to cataract surgery, but preoperative treatment with either laser and/or anti-VEGF medications may be warranted [50].

Combined cataract surgery and PPV can be done when the view to the retina is suboptimal from the dense cataract [51]. In these surgeries, it is particularly important to minimize phacoemulsification energy to keep the cornea as clear as possible for the retina surgery. Additionally, a more rigid three-piece intraocular lens and placing of a corneal suture at the main cataract incision can help keep the intraocular lens

and globe stable during and following retinal surgery. There are varying views on the timing of intraocular lens—before vitrectomy or afterward. Placing the intraocular lens at the end of the procedure allows an improved view of the periphery through an aphakic eye and may be advantageous in anterior dissections [51].

5.2.4.2 Asteroid Hyalosis

Media opacities such as asteroid hyalosis may also limit or prevent adequate treatment of diabetic retinopathy (Fig. 5.5). In some instances, it may be necessary to perform a vitrectomy to improve the view in order to optimize treatment and attempt to preserve vision prior to the development of further complications.

5.3 Preoperative Considerations

5.3.1 Systemic Optimization

Patients with diabetic retinopathy requiring surgery are a difficult group to treat given they can be systemically unwell with multiple medical comorbidities. The 5-year survival of patients undergoing diabetic vitrectomy ranged from 68% to 86%, especially in the presence of coexisting heart and renal disease [52–57]. A more recent study showed that in this population, 39% have a history of stroke, 28% have a history myocardial infarction, and 43% have a history of renal failure [58]. In addition, many patients require anticoagulation and antiplatelet therapy, and the decision of whether to hold these

medications prior to surgery must be made in conjunction with the patient's primary care physician and/or cardiologist. Medical clearance by an internist and the anesthesiologist is recommended to ensure that the patient's health is optimized so they can more safely undergo surgery.

5.3.2 Ancillary Testing and Patient Expectation

In the case of media opacity such as vitreous hemorrhage, cataract, or hyphema, B-scan ultrasonography can be crucial to maximize preoperative clinical information to determine the surgical plan. The B-scan can reveal areas of traction, rhegmatogenous detachment, or anterior hyaloid fibrovascular proliferation [2] (Fig. 5.6).

In cases where there is a view, fluorescein angiography and, more recently, optical coherence tomography angiography can show macular ischemia which may limit ultimate vision despite anatomically successful surgery and the absence of macular edema. Structural optical coherence tomography showing integrity of the external limiting membrane and ellipsoid zone has also been shown to correlate well with postoperative best corrected visual acuity, while central foveal thickness and enlarged foveal avascular zone only exhibit a weak correlation [58].

Even with anatomically successful results, ultimate vision postoperatively may be limited by ischemia from chronic microvascular disease or atrophy from chronic anatomic abnormalities [6]. Patient expectations must be managed preoperatively. These various imaging modalities can often

be helpful to establishing realistic patient expectations prior to going into surgery.

5.3.3 Preoperative Anti-VEGF

Prior to doing surgery, many providers will inject intravitreal anti-VEGF agents to minimize or eliminate progressive bleeding; however, in patients with underlying traction, the rapid regression of neovascular tissue can theoretically cause a "crunch phenomenon" [2], leading to new or worsening tractional detachments at a mean of 13 days following injection [59–63]. However, in the recently published DRCR.net protocol S trial, no patients were seen to experience the "crunch phenomenon" [64]. There is limited published evidence to guide the use of preoperative anti-VEGF, but expert opinion suggests limiting anti-VEGF to within 3 days of surgery and only in patients medically cleared for surgery [2, 6, 51, 65].

5.4 Surgical Techniques

In recent years, new preoperative and intraoperative instrumentation and surgical techniques have improved the manner in which retinal specialists treat diabetic retinopathy. The surgical goals for diabetic vitrectomy include removing any media opacities, relieving traction, removing or segmenting preretinal membranes, drainage of fluid through retinal holes or breaks when present, endolaser around breaks and for panretinal photocoagulation to decrease neovascular drive, and the placement of tamponade agents such as gas or silicone oil, if needed.

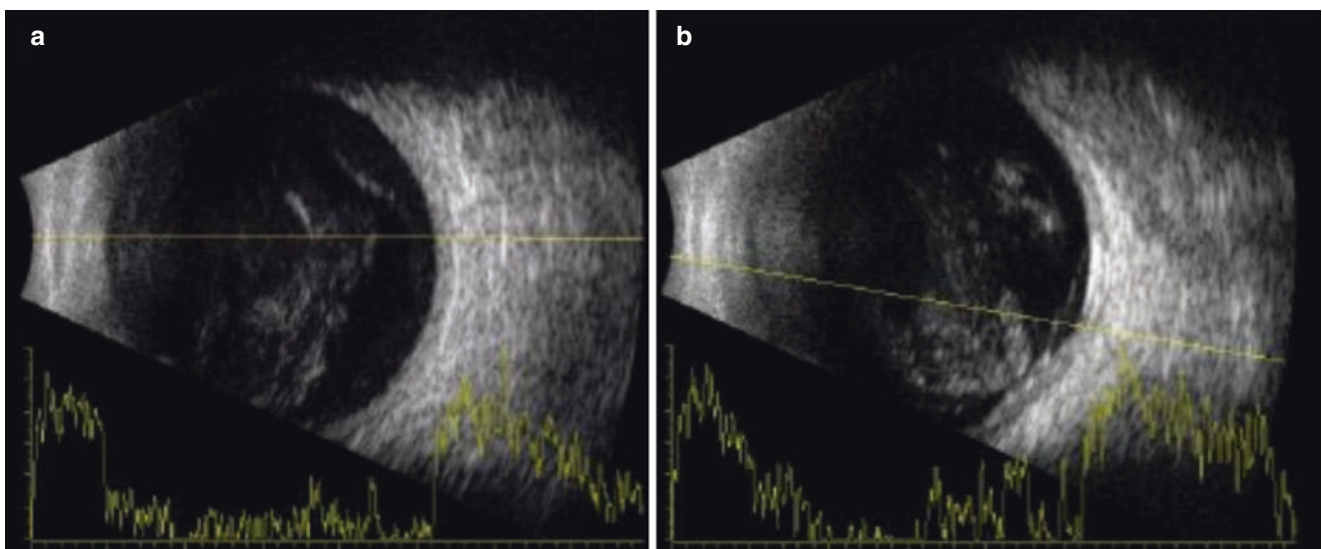


Fig. 5.6 This patient presented with a dense vitreous hemorrhage with no view to the posterior pole. B-scan ultrasonography showed a vitreous hemorrhage (a) with questionable area of traction inferotemporally (b)

A good vitrectomy is crucial in diabetic surgery. The typical diabetic vitreoretinal interface is abnormal. Triamcinolone acetonide can be used intraoperatively to better visualize the vitreous, especially in the case of vitreoschisis. Afterward, two general techniques are used to address fibrovascular membranes: segmentation and delamination.

1. *Segmentation* involves the vertical cutting of membranes between areas of retinal adherence into small segments either with the vitreous cutter or vertical scissors. The remaining fibrovascular stumps are then trimmed with the vitreous cutter leaving behind small, circumscribed remnants centered on neovascular pegs. Segmentation is necessary in situations where removal of the fibrovascular membrane is impossible or too risky due to tight adherence or mobile retina. The disadvantage of segmentation is the residual islands of fibrovascular tissue that can proliferate and bleed.
2. *Delamination* involves completely separating the vitreoretinal adhesions between the retina and fibrovascular proliferation either with peeling, horizontal scissors, a pick, or hydro-/viscodissection to gently remove the tissue from the retina. Diathermy may be needed in these cases to cauterize neovascular pegs to limit bleeding. The disadvantage of this technique is excessive hemorrhage and the risk of iatrogenic retinal tears if performed too aggressively [66]. Dyes such as indocyanine green, brilliant blue G, and trypan blue can be used to highlight preretinal membranes that cause traction.

Ultimately, endolaser photocoagulation is essential in the face of active neovascularization to decrease the neovascular drive and to circumscribe any areas of retinal breaks. In a prospective study of 174 consecutive vitrectomies, 39% of eyes were found to have a retinal break. In 27%, the breaks were posterior and occurred during membrane dissection, whereas 17% of eyes had entry site breaks [67].

Long-term tamponade such as gas or silicone oil can also be helpful in cases where there are multiple and/or large retinal defects, whether they were present preoperatively due to traction or created intraoperatively during retinal manipulation. In one study, 49% of eyes required internal tamponade, with air used in 8% of eyes, SF₆ gas in 24%, C₃F₈ gas in 10%, and silicone oil in 7% [22]. The use of silicone oil can also reduce the risk of postoperative phthisis in combined tractional-rhegmatogenous retinal detachments [20, 68]. Even in the absence of retinal breaks, the use of intraocular gas tamponade has been proposed to reduce postoperative hemorrhaging, albeit with variable results [69, 70]. In the case of silicone oil use, water-soluble growth factors can reach high concentrations in the thin fluid film between the retina and the silicone bubble, and consequently there can

be an increased tendency for fibrovascular re-proliferation. Any sub-silicone oil fibrosis can be removed with silicone oil exchange or by direct peeling under silicone oil.

Modern vitrectomy machines have cut rates over 10,000 and a wide range of flow options [71]. High-cut rates with low aspiration allow for precise cutting in close proximity to the retina, resulting in reduced risk of retinal tear formation. The use of small gauge instrumentation with 25- or 27-gauge instruments can also provide precise segmentation and delamination of fibrovascular tissue without the use of multiple instruments [72]. With certain machines, the option of proportional reflux can be used for hydrodissection or viscodissection of preretinal fibrovascular plaques. Also, a bimanual technique, after placement of a chandelier or with use of lighted instruments, can be helpful, especially with strongly adherent fibrovascular tissue on a detached retina. A variety of instrumentation such as flex loops, retinal forceps, and retinal scissors are available for use offering numerous options for segmentation and delamination.

Mixed gauge surgery is also an option where 23- or 25-gauge trocars are used in conjunction with 23-/25- and 25-/27-gauge instrumentation. 27-gauge cutters can be advantageous in reaching tight spaces between preretinal membranes and retina and offer more precise maneuverability [2]. For more peripheral pathology or in situations where a stiffer instrument is needed, 23-/25-gauge instruments can still be used. Smaller gauge surgery with 27-gauge instrumentation has been shown to have lower intra- and postoperative complications with less bleeding, iatrogenic breaks, and hypotony [73].

Intraoperative OCT is a novel imaging technology that allows the surgeon to view real-time cross-sectional microstructure of the retina and vitreoretinal surface. The technology is still evolving but can be used in complex cases to help identify tissue planes, subclinical epiretinal- or internal-limiting membranes, subclinical detachments, and diagnosis of inadvertent macular hole formation [2, 6, 51, 74].

5.5 Surgical Complications

The first study on diabetic vitrectomy, DRVS, had a high complication rate with 20% of patients losing light perception vision [75]. The introduction of better visualization and illumination, diathermy, small gauge surgery, valved cannulas, and improved surgical techniques and instrumentation have drastically decreased the complication rate.

5.5.1 Intraoperative Complications

Maintaining hemostasis is an important concept in all of intraocular surgery; however, it is of particular importance in diabetic vitrectomy given the propensity for these eyes to

bleed given the fragile vessels and adherent fibrovascular tissue. Modern vitrectomy machines and packs include valved cannulas and the ability to control intraocular pressure, allowing hemostasis without using excessive diathermy. In addition, appropriately timed preoperative intravitreal anti-VEGF can also reduce the likelihood of intraocular bleeding from neovascularization [6].

In cases of dense vitreous hemorrhage where the chronic hemorrhage can be very thick, the vitreous can wrap around the vitrectomy cutter when passed through the cannulas. If this vitreous is not sufficiently removed before retracting the cutter, the extraneous vitreous can lock the cutter in the cannula, and any subsequent forceful pulling can dislodge the cannula with the vitrector causing significant traction leading to adjacent retinal tears [6]. Extra care must be taken to identify and treat any inadvertent tears that may be created during the surgery.

Similarly, the tight abnormal posterior hyaloid adhesion to the retina predisposes the retina to iatrogenic tears and retinal detachments, especially in maneuvers that emphasize anterior-posterior traction. The rate of iatrogenic tears has been reported to range from 20% to 41% [22, 24, 76, 77]. If found, traction adjacent to the retinal breaks should be relieved and the breaks then encircled with endolaser.

Loss of adequate visualization can make any PPV difficult. This is particularly important in diabetic vitrectomy given the challenging and sometimes lengthy nature of the surgery and the need to have intermittent intraocular pressure elevation to achieve hemostasis. Therefore, intraoperative corneal edema and osmotic cataract can be real concerns [78]. Occasionally, removal of the corneal epithelium is necessary to improve intraoperative view [79]. While corneal epithelium in healthy individuals regenerates within days, the epithelial defect in patients with diabetes can become a non-healing corneal abrasion requiring bandage contact lens placement and antibiotic care to prevent against discomfort and corneal ulcers, scars, and even melt [79, 80]. Adding 50% dextrose to the BSS infusion bottle can help prevent loss of view from the lens in phakic patients [81].

Prior to the advent of small incision vitrectomy, vitreous and retinal incarcerations at the site of large sclerotomy wounds were also possible. These large sclerotomies also allowed for fibrovascular ingrowth in extremely ischemic eyes, and manipulation without cannulas would induce vitreous traction and lead to subincisional retinal tears [73]. This, fortunately, is much less common with advances in modern vitrectomy.

5.5.2 Postoperative Complications

5.5.2.1 Vitreous Hemorrhage

Vitreous hemorrhage is a common postoperative complication, occurring in 5–63% of eyes, almost half presenting on the first postoperative day [22, 63, 82–87]. Immediate post-

operative hemorrhage, often called “shake-out” hemorrhage, usually resolves spontaneously over a few weeks. Periodic ultrasonography in the case of no retinal view should be performed to exclude a retinal detachment, which would require prompt surgery given rapid progression in a post-vitrectomized eye. Early postoperative hemorrhage typically results from dispersion of difficult to remove blood from the peripheral vitreous skirt and from inadequately diathermized vessels and fibrovascular complexes, which can be further exacerbated by postoperative hypotony or changes in intraocular pressure during sclerotomy closure [87]. Causes of late postoperative hemorrhage include fibrovascular ingrowth into sclerotomies as noted above, more common prior to small gauge vitrectomy [88–91], and persistent neovascularization from residual fibrovascular tissue [85]. Variable evidence exists for whether preoperative anti-VEGF decreases the risk of postoperative bleeding with some studies supporting no benefit [63, 85] and some studies reporting a reduction in early postoperative bleeding [82].

5.5.2.2 Retinal Detachment

A rhegmatogenous retinal detachment (RRD) extending from the periphery is uncommon in the presence of existing panretinal photocoagulation and is more likely to be found posterior due to unrecognized retinal breaks. The rate of postoperative detachments has been found to range from 4.3% to 8.1% [76, 92, 93]. The risk of RRD following diabetic vitrectomy appears to be declining, probably due to the use of wide-angle viewing systems, which allow for more accurate examination of the peripheral retina [93].

5.5.2.3 Cornea

The incidence of corneal complications following a diabetic vitrectomy has been reported to be as high as 50% [94] and can be due to delayed epithelial regeneration and abnormal neurotrophic status [95]. Additionally, diabetics have been found to have structurally and functionally abnormal corneal endothelial cells that are susceptible to damage and this can translate to the health of the corneal epithelium which require the endothelial pump to remain healthy [96–98]. The use of silicone oil in complicated detachments can also lead to band keratopathy.

5.5.2.4 Miscellaneous

- Expedited cataract progression following diabetic vitrectomy is common and should be promptly treated not only for visual rehabilitation but also to allow adequate examinations of the retina.
- Postoperative epiretinal membranes in eyes with appropriate visual potential can undergo subsequent surgical management if they cause visually significant distortion or blurry vision.

- Elevated intraocular pressure can happen after any intraocular surgery either due to endotamponade agent or by obstruction of the ocular drainage system; however, diabetic optic nerve heads have also been found to have impaired flow autoregulation that makes them especially prone to changes in intraocular pressure [99].

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