

An update on the management of diabetic tractional retinal detachment



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Dates:

Received: 08 May 2022
Accepted: 12 June 2022
Published: 30 Aug. 2022

How to cite this article:

Hajee A, Makgotloe MA. An update on the management of diabetic tractional retinal detachment. *Afr Vision Eye Health*. 2022;81(1), a774. <https://doi.org/10.4102/aveh.v81i1.774>

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Background: Tractional retinal detachment (TRD) occurs when contractile forces in the vitreous and neovascular tissue lead to the detachment of the neurosensory retina. The pre-operative use of anti-vascular endothelial growth factor (anti-VEGF) and advances in microsurgical instrumentation, such as a small gauge vitrectomy (SGV), have improved surgical outcomes.

Aim: The purpose of this review is to highlight recent trends in the management of diabetic TRD, supporting earlier surgical intervention and the expanded surgical indications.

Methods: PubMed was searched for the following terms: 'diabetes' OR 'diabetic retinopathy' AND 'TRD' AND 'pars plana vitrectomy (PPV)' AND 'anti-VEGF' AND 'endophotocoagulation'. Reference lists were reviewed for additional articles. The review was focused on all articles later than 2010 for recent updates on the ever-changing management of this disease entity. No case reports were included in this review article.

Results: Management of TRD continues to remain challenging, despite the recent advancements in techniques and instrumentation. Each case needs to be individualised, with careful pre-operative planning, understanding of patient expectations and counselling, coupled with meticulous surgical skills and diligent postoperative management.

Conclusion: Management of TRD continues to remain challenging despite recent advances in techniques and instrumentation. Vitrectomy for TRD can improve vision-related quality of life, and the continued evolution and improvement in surgical techniques and adjunctive pharmacotherapy will most likely continue to improve postoperative outcomes.

Contribution: The paper presents an overview of current management of tractional retinal detachment in patients with advanced proliferative diabetic retinopathy.

Keywords: diabetes; diabetic retinopathy; tractional retinal detachment; pars plana vitrectomy; anti-vascular endothelial growth factor; endophotocoagulation.

Introduction

End-stage diabetic retinopathy is an important cause of new blindness in the adult population. Risk factors for vision loss include vitreous haemorrhage (VH), retinal neovascularisation and angiogenesis. Tractional retinal detachments (TRDs) occur when contractile forces in the vitreous and neovascular tissue lead to the detachment of the neurosensory retina. Important considerations need to be taken into account when managing diabetic patients who present with this challenging diagnosis.

Pathophysiology of tractional retinal detachments

Uncontrolled systemic hyperglycaemia activates pathways that cause capillary closure, retinal ischaemia and subsequent breakdown of the vascular basement membrane.^{1,2} This initial insult increases the production of angiogenic factors such as vascular endothelial growth factor (VEGF), the upregulation of pro-inflammatory chemokines and cytokines and elevation of nitric oxide levels.^{1,3} The complex interaction between these factors plays a prominent role in fibrous tissue proliferation and fibrovascular membrane formation. The interplay between this and tractional forces at the sites of vitreoretinal attachments can lead to VH as well as TRDs.^{1,2,3}

Types of tractional detachments

There are many different ways of categorising TRDs. Most surgeons divide them into either macula-involving or non-macula involving TRDs. Kroll et al. classified them from A to D:⁴

Type A: A flat retina with proliferative changes in the vitreoretinal interface. Vision loss in this type is either caused by macula oedema or VH.

Type B: Extramacular TRDs but with more prominent macula oedema and a worse visual outcome.

Type C: A TRD involving the macula but with an attached fovea.

Type D: Complete TRD involving the whole macula. Types C and D are thought to have the worst prognosis.²

Surgical indication

Surgery for these clinically complex cases is indicated when the benefit to risk ratio is higher. The greatest surgical risk is that of iatrogenic retinal breaks.² The two common anatomical indications for surgery in TRD are: (1) a TRD threatening the macula (where the area of retinal elevation is at least 4 disc diameters and within 30 degrees of the macula centre or if the elevation is less than 4 disc diameters but includes one or more vitreoretinal adhesions within 30 degrees of the macula centre, plus a new vessel or a fresh VH); (2) a TRD involving the macula (where there is vitreoretinal traction through the fovea, along the arcades or at the disc, which causes visual loss).²

Surgery is also indicated for those TRDs that are present for less than six months' duration. Patients who have TRD that is longstanding (more than six months) often have strongly adherent fibrous membranes, photoreceptor degeneration and an atrophic retina and are thus very challenging cases with little to no postoperative useful vision.^{1,2}

Extramacular TRDs can be treated with panretinal photocoagulation, referred for risk factor reduction and observed and re-evaluated for surgical candidacy. Indications for repair of extramacular TRDs include fibrovascular proliferation with macula traction, vitreous traction involving the optic nerve and the inability to halt fibrovascular proliferation with clinic-based procedures.^{1,2,3}

A combined tractional-rhegmatogenous retinal detachment is also a relative indication for repair, although these types of cases are technically very challenging and have a variable prognosis following surgery.³

With advances in instrumentation and surgical techniques, indications to repair TRD have also broadened to include severe fibrovascular proliferation causing tractional macula oedema and fibrovascular tissue causing media opacities. Studies have shown that patients with the greatest severity of neovascularisation benefitted the most from early vitrectomy.^{1,2}

Pre-operative planning

Slit lamp examination

A comprehensive dilated fundus examination using a binocular indirect ophthalmoscope is essential for accurate

surgical planning in the management of TRD. Preoperative visual acuity generally correlates with postoperative visual outcomes.^{1,3} Iris neovascularisation increases the risk of postoperative poor vision. Care should be taken to examine the posterior vitreous and its sites of attachments from the optic nerve and retinal vessels. The vascular arcades should also be examined for areas of ischaemia. The surgeon should note the anterior extent of the detachment, which can extend from the posterior pole to anterior to the equator. The larger the extent of the retinal detachment, the higher the likelihood that it is accompanied by a severe vitreoretinal adhesion. These patients may require a more experienced surgeon, widefield viewing techniques and the use of bimanual surgery. They also carry a lower postoperative visual prognosis because of higher incidence of developing iatrogenic tears.^{1,2}

Investigations

The use of imaging modalities is important for prognostication and patient counselling. The topography of the detachment can also be assessed, and this can assist in making the decision to surgically intervene and pre-operative planning.²

B-scan ultrasonography is helpful in cases presenting with an opaque media, such as a dense cataract or VH, and it can help differentiate between a posterior vitreous detachment (PVD) and a vitreoschisis.² It may also aid in differentiating peripapillary proliferation from preretinal proliferation, which carries a poorer prognosis.

Macular ocular coherence tomography (OCT) can distinguish between macula and non-macula involving TRD and help to distinguish between TRD and tractional retinoschisis.^{2,5} Real-time intra-operative OCT can assist in the identification of dissection planes, residual tractional bands, retinal breaks and retinoschisis intra-operatively.^{5,6}

Ocular coherence tomography angiography (OCT-A) can assess the integrity of the foveal avascular zone and correlate such findings with intravenous fluorescein angiography findings. This is important for preoperative assessment of prognosis and discussion with patients.^{5,6} Widefield swept source OCT-A provides *en face* angiograms of the entire posterior pole, which can assist with surgical manipulation of the fibrovascular membranes. This can help the surgeon to avoid transection of the highly fragile and vascular membranes.⁶ Ocular coherence tomography angiography imaging can also assist in the longitudinal evaluation and postoperative follow-up by measuring the foveal avascular zone and thus analysing the reperfusion status of the retina.^{2,6}

Patient selection

The selection of patients for surgery should always have a greater benefit-to-risk ratio. Patients should be counselled about the risk of developing iatrogenic retinal breaks, poor visual outcomes in some instances and long-term follow-up times.^{2,7}

Historically, TRDs' repair was only indicated in tractional detachments that involved or threatened the macula. Extramacular TRDs were generally observed or treated with panretinal photocoagulation, but newer studies suggest that there is a higher rate of success and an increased quality of life for patients whose TRD is managed with pars plana vitrectomy (PPV) than with observation alone. This is likely because of the advancements in microsurgical techniques, skills and instrumentation.^{4,7}

Patient demographics may play a role in the postoperative visual outcomes. In one study, patients of African descent lost vision postoperatively because of extensive vitreoretinal adhesions, while white and Asian patients' vision improved. Low-income Latino patients had more advanced disease on presentation and had poor compliance with postoperative positioning and follow-up. This had a direct relationship with their visual recovery and outcome.² Other studies did not show this correlation between race and visual prognosis but instead attributed these outcome differences to variables such as poorer standard of living.

Age has been reported as a possible predictor of surgery outcome, with younger patients having better visual outcomes despite presenting with more advanced disease. This might be attributed to their healthier optic nerve.²

Pre-operative antivasular endothelial growth factor

Intravitreal antivasular endothelial growth factor (anti-VEGF) therapy is known to be effective at decreasing vascular permeability and proliferation, improving macular oedema and decreasing the risk of intraocular bleeding in patients with proliferative diabetic retinopathy (PDR).^{8,9} A meta-analysis by Zhao et al. reported that the preoperative use of bevacizumab decreases the risk of intra-operative haemorrhage, assists in the dissection of fibrovascular membranes and reduces the risk of intra- and postoperative complications.¹⁰ Other reports have suggested that the use of intraoperative bevacizumab (IVB) may cause TRD. Arevalo et al. concluded that adjuvant pre-operative IVB can decrease intra-operative bleeding, improve the surgical field of view and reduce the risk of iatrogenic retinal tears; however, they did not show an improvement in best corrected visual acuity (BCVA) in the study versus the control group.⁸

A major review by Iyer et al. reported that pre-operative IVB reduces intra-operative bleeding, iatrogenic retinal tears and the need for relaxing retinotomies. These patients are also more likely to have an air tamponade than a silicone oil tamponade.²

Intra-operative bevacizumab can also make vitrectomy surgery relatively easy, in some instances reducing the surgical time to about 26 min. This has been attributed to having fewer vascular membranes to dissect and the ease with which the posterior vitreous and fibrovascular membranes are separated from the retina. Patients in whom IVB was injected pre-operatively also did not need intra-operative laser, thus also contributing to a shorter surgical duration. According to this

review, patients also had better visual outcomes at one and six months postoperatively. It was also observed that even though IVB had improved outcomes in patients with a TRD, in patients without one, it caused progression to TRD as early as three days post injection, increased the risk of subretinal bleeding and contributed to the development of combined rhegmatogenous retinal detachments (RRDs).²

Panretinal photocoagulation

In patients with TRD, the use of pre-operative PRP is questionable. It could not only lead to improved visual outcomes but also has the risk of contributing to the development of retinal tears, caused by the high voltage laser energy used and inflammation caused by the contraction of the membranes. Extensive PRP scars can also cause tight vitreoretinal adhesions, making surgical removal of retinal membranes more difficult.²

Pre-operative medical management

Patients with TRD often have uncontrolled hyperglycaemia and renal dysfunction, which often contributes to their poor systemic clinical outcomes. The survival of these patients has been reported to be as low as 2.7 years following TRD repair.

The prompt referral to an endocrinologist is very important, as poor blood sugar control and renal dysfunction are directly related to a worse postoperative visual outcome. Patients who were put onto statins and insulin pre-operatively seemed to have better visual outcomes, and endocrinologists can assist in instituting these systemic treatments.²

Surgical approaches

Field of view

Good visibility is very important in the surgical management of TRD. Peripheral vitreous removal is facilitated by good pupillary dilation, but widefield viewing systems allow for visualisation through small pupils. Some surgeons use iris hooks or intracameral epinephrine to improve visualisation of the peripheral retina.^{1,2}

Widefield viewing allows for visualisation of the peripheral retina and reduces the risk of retinal redetachment, most probably by improving the visibility of peripheral retinal tears. Non-widefield contact lenses provide high quality, large magnification of dissection planes for precise instrument placement. Disadvantages include not having a view of the periphery and the need for an assistant.^{1,2}

Light options include chandeliers or a light-pipe. Chandeliers should be used when bimanual manipulation of the tissues are needed. They also decrease light toxicity, as they are further away from the retina.^{1,2}

Cataract removal

Combining cataract extraction and vitrectomy remains controversial. Some studies suggest an increased risk of

neovascularisation of the iris and neovascular glaucoma in the diabetic patient. Corneal oedema may also ensue because of lengthier surgical times. There is also a greater likelihood of postoperative inflammation and uveitis after a phacovitrectomy for TRD. Some reported advantages of this combined phacovitrectomy surgery include having a single surgery, earlier vision improvement and better postoperative visualisation of the retina. Some prospective studies report that combined phacovitrectomy has similar reattachment rates, similar postoperative neovascularisation of the iris (NVI) formation but better visual acuity at six months than patients who are treated with PPV alone.^{2,3}

Selection of gauge size

Gauge selection is mainly based on the difficulty of the surgical case and surgeon preference. The 25- and 23-gauge systems are generally used because of their quick wound recovery, lesser conjunctival scarring, shorter theatre times, decreased postoperative inflammation and reduced iatrogenic corneal astigmatism. Patients also have improved comfort and visual recovery.⁷

Newer 27-gauge technology is advantageous because it offers higher cut-rates, which assist in the dissection and shaving of fibrovascular membranes and rarely cause complications such as VH and transient hypotony.¹¹

Even with the improvement of gauge selection, some surgeons still prefer lower-gauge bimanual membrane dissection for larger sites of vitreoretinal attachment.^{1,11}

Bimanual surgery

Segmentation and delamination

In TRD, fibrovascular membranes are tougher than the retina, and so peeling of the membranes can cause iatrogenic retinal tears. Bimanual removal allows for a safer dissection with better manipulation of the surgical plane.^{1,2}

Segmentation allows for the separation of adherent tissues into small segments to be managed individually around the neovascular epicentre and dissected off the retinal surface.⁶ Prior to the removal of the membranes, the vitreous cortex should be excised from the mid vitreous, away from the posterior vitreous. The posterior vitreous cortex is then incised away from the retina and separated circumferentially before dissection of adherent membranes.^{1,2}

En bloc resection

In the original *en bloc* technique, the posterior vitreous is left intact and vitreoretinal traction is used to lift both the posterior vitreous and fibrovascular membranes, which can be incised with scissor. Unfortunately, this technique increases the risk of iatrogenic tears. Many modified *en bloc* techniques now exist, where the surgeon can proceed to delamination first. The preretinal fibrovascular membrane can then be removed in bulk, alternating its removal with blunt dissection and the use of scissors.²

Removal of internal limiting membrane

Removal of the internal limiting membrane (ILM) is performed to abolish the scaffold for future membrane formation. It ensures the removal of preretinal membranes and overlying vitreous remnants. It also increases the postoperative rate of macular pucker and macular oedema.²

Endophotocoagulation

Endo laser can be placed to the retinal pigment epithelium after the retina is reattached, in cases of retinal tears or a combined RRD-TRD.

Furthermore, PRP can also be applied postoperatively, as the retina is reattaching. It can be given through silicone oil or gas. Adequate endo laser prevents macular redetachments from sclerotomy-associated tears.^{2,3}

Choice of tamponading agents

There are currently no strict guidelines for the use and type of tamponading agents for TRD. Silicone oil is usually used for severe, complex pathologies, with larger inferior retinotomies requiring long-term tamponade. Silicone oil is stable in the vitreous cavity for up to one year; however, this can cause decreased postoperative visual acuity, band keratopathy, great risk of cataract formation and intraocular pressure (IOP) spikes. Posterior breaks or a combined TRD-RRD are relative indications for the use of silicone oil. It is also preferred in circumstances where patients cannot adopt special postoperative head positions because of being physically handicapped.^{2,3,12}

Long-acting C3F8 has been used with prolonged face-down positioning; visual recovery has been reported to be better than patients with silicone oil tamponade, and there are fewer postoperative complications. It is also preferred by some surgeons because of its increased surface tension and buoyant forces compared with silicone oil, as well as having the advantage of spontaneous reabsorption.^{3,12}

Perfluorohexyl octane (F6H8) has been reported as a possible tamponade for TRD and other complex cases, but higher incidence of complications such as redetachments, phthisis bulbi, hypotony and retinal scarring have been reported, and these limit its use.^{3,12}

Intra-operative antivascular endothelial growth factor

Intra-operative anti-VEGF agents such as bevacizumab improve visual outcomes by blocking the PPV-induced VEGF surge, with resultant decrease in the incidence of postoperative VH.⁹

Complications

Intra-operative

Common intraocular complications range from iatrogenic retinal tears to difficulty with haemostasis. These can be

caused by the use of large gauge vitrectors and the non-use of VEGF agents. Complications such as vitreous incarceration or fibrovascular ingrowth occur because of large and poorly constructed vitrectomy ports.^{1,7}

Postoperative complications

Vitreous haemorrhage

Postoperative VH is a major complication, which can be mitigated with the use of pre- or intraoperative anti-VEGF agents. Vitreous haemorrhage generally resorbs spontaneously and nonresolving haemorrhages were associated with poor glycaemic control.

Vitreous haemorrhage can be classified into early (within one week of surgery) or delayed VH (occurring three months after surgery).^{2,7}

Early VH usually clears spontaneously within 2–6 weeks, without any intervention. Delayed VH affects 10% – 20% of patients and is caused by residual fibrovascular membranes and fibrovascular ingrowth at the sclerostomy site. It can be prevented by using laser photocoagulation or cryotherapy to the peripheral retina and sclerostomy site.^{2,7}

Redetachments and proliferative vitreoretinopathy

Rhegmatogenous retinal detachment occurs in about 5% of cases, which results from peripheral or posterior breaks. This can lead to the formation of proliferative vitreoretinopathy (PVR) with associated retinal redetachment and anterior segment neovascularisation.^{2,7}

Cataract formation

With the advent of small gauge vitrectomy (SGV), iatrogenic cataract formation has become uncommon. Nuclear sclerosis and posterior subcapsular lens opacities can occur, commonly after lens touch or prolonged gas tamponade. In studies that looked at outcomes of TRD surgery, cataract formation typically occurred in 25% of patients after two years and progressed slower in diabetics than nondiabetics, likely because of lower oxygen tension or hyperglycaemic rate in the former.²

Intraocular pressure control

High IOP is caused by an increased oxidative stress in the anterior chamber following vitrectomy surgery, which leads to damage of the trabecular meshwork.⁷

Neovascular glaucoma

This results from high-circulating angiogenic factors, which reach the anterior chamber via a concentration gradient. This can be prevented by the use of pre- and intraoperative anti-VEGF agents.⁷

Hypotony

Hypotony is a common immediate complication after SGV, with a reported incidence of 16%. This can be avoided using

oblique sclerotomies, a tamponading agent and suturing the site of sclerotomy leakage.^{2,7}

Special circumstances

Combined tractional retinal detachment-rhegmatogenous retinal detachments

In a combined TRD–RRD, a retinal break may be obscured by a fibrovascular membrane, a retinal fold or VH. Poor pre-operative visual acuity, NVI and macular detachment are predictors of a poor prognosis; however, the use of anti-VEGF agents and improved microsurgical instruments have improved the outcomes in these patients.^{2,9}

Co-existing macular holes

Macular holes can either be caused iatrogenically when removing membranes from the macular or rarely develop from tangential traction from the posterior vitreous and ILM complex. Either way, they do not have different visual outcomes when compared with patients who have primary TRD without macular holes.²

Visual outcomes

Positive elements for visual recovery after vitrectomy for macular-involving TRD include a short duration of detachment, previous treatment with panretinal photocoagulation (PRP) and the absence of both VH and severe neovascularisation.¹

Quiroz-Reyes et al. demonstrated that the disorganisation of retinal inner layers (DRIL) on OCT imaging is a very strong and distinct biomarker that can indicate tissue damage and lower likelihood of tissue recovery.⁵ They reported that patients who had increased DRIL length on OCT imaging had less viable remaining tissue and poorer visual outcomes, even in successfully treated TRD involving the macula.^{1,5} Longer studies with fewer confounding variables are needed to give a better understanding of visual outcomes in TRD surgery.

Conclusion

The management of TRD continues to remain challenging despite the recent advancements in techniques and instrumentation. Each case needs to be individualised, with careful pre-operative planning, understanding of patient expectation and counselling, coupled with meticulous surgical skills and diligent postoperative management.

Vitrectomy for TRD can improve vision-related quality of life and it is to be hoped that the continued evolution and improvement of surgical techniques and adjunctive pharmacotherapy will continue to improve postoperative success rates.

Acknowledgements

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

A.H.'s contribution includes project conceptualisation and design, data collection and analysis and write-up of the manuscript. M.A.M.'s contribution includes project conceptualisation and design, data analysis, review the manuscript, supervision of the project and funding acquisition.

Ethical considerations

Ethical approval and permission to conduct the study were obtained from the Human Research Ethics Committee (Medical) at the University of the Witwatersrand (ref. no. M141195).

Funding information

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability

Raw data of this research are available on request from the corresponding author.

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The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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