Recognising and managing diabetic retinopathy

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Key learning points
• Detecting and diagnosing diabetic retinopathy is not complicated. There are clinical signs which can be seen with an ophthalmoscope or a slit lamp and 90- or 78-dioptre lens.
• Diabetic retinopathy is treatable. Treatment usually maintains vision, but does not restore vision that has already been lost.
• In diabetic maculopathy, laser or anti-VEGF injections are both proven to work. Intravitreal steroid is ineffective in most patients.
• Laser treatment should use small spots and just enough power to produce a visible reaction.
• Proliferative retinopathy is best treated with pan-retinal laser. The commonest error is undertreatment, and laser should be applied until there is regression of the new vessels or there is no room for further treatment.
• Vitrectomy is useful for vitreous haemorrhage and late complications of proliferative retinopathy. Pre-treatment with bevacizumab reduces the risk of surgical complications.

Recognising DR
The management of diabetic retinopathy (DR) depends on accurately recognising or classifying the different types of DR and knowing what treatment to give the patient.

DR has clinical signs which can be seen with an ophthalmoscope or with a slit lamp and a 90- or 78-dioptre lens. The advantage of the slit lamp is that it allows you to visualise the retina with both eyes. This stereoscopic vision provides a sense of depth which aids diagnosis, particularly of macular oedema. Other aids to DR diagnosis are fundus photography, fluorescein angiography, and optical coherence tomography (see box on page 7).

1 Non-proliferative DR
The clinical signs of non-proliferative DR are:
• haemorrhages (Figure 1)
• microaneurysms (Figure 1)
• venous beading (Figure 2)
• intraretinal microvascular abnormalities (IRMA) (Figure 3)

2 Proliferative DR
Proliferative DR can exhibit all the same clinical signs as non-proliferative DR. However, the key characteristic of proliferative DR is new vessels growing onto the posterior vitreous surface from the retina or optic disc (Figure 4).

The new vessels damage sight by bleeding (Figure 5) or forming sheets of fibrovascular membranes that may cause traction retinal detachments. Traction retinal detachment occurs when the fibrovascular tissue contracts and pulls the retina away from the underlying choroid. If this affects the macula, the central vision will be lost.
3 Diabetic maculopathy

Diabetic maculopathy occurs when DR affects the central part of the retina. Blood vessels leak, leading to diabetic macular oedema (swelling of the retina).

The early treatment of diabetic retinopathy study (ETDRS) defined clinically significant macular oedema (CSMO) as the stage at which the eye needs to be treated in order to prevent loss of vision. The definition depends on recognising the following:

- retinal thickening and exudates (Figure 6) at or within 500 microns of the fovea (within one third of a disc diameter).
- larger zones of retinal thickening (one disc diameter or more), if within one disc diameter of the fovea.

Retinal thickening can only be observed stereoscopically. So, for practical clinical purposes, look for other easily visible markers for macular oedema such as exudates within a disk diameter of the fovea.

The blood vessels in the central part of the retina may also become blocked (capillary closure), leading to macular ischaemia. Macular ischaemia occurs when there is insufficient blood supply to the macula. This will impair the normal functioning of the retina, leading to reduced vision.

There is no effective treatment for macular ischaemia, but it is important to recognise it so that you don’t waste the patient’s time and money with ineffective laser or anti-vascular endothelial growth factor (anti-VEGF) treatment.

Although macular ischaemia can only be diagnosed conclusively by fluorescein angiography (see box on page 7), you should suspect it if the following conditions are met:

- reduced visual acuity
- evidence of retinal ischaemia, e.g. cotton wool spots (Figure 7) or blot haemorrhages
- no macular oedema at the fovea
- no other cause for reduced vision (e.g. cataract, refractive error).

### Diabetic vitrectomy

Vitrectomy is indicated in proliferative diabetic retinopathy in the following conditions:
non-clearing vitreous haemorrhage
pre-retinal (or sub-hyaloid) haemorrhage
tractional retinal detachment threatening, or involving, the macula
combined rhegmatogenous/tractional detachment
progressive severe fibrovascular proliferation in spite of adequate PRP

Currently, vitrectomy for diabetic macular oedema is reserved for the few patients who have vitreous traction on the macula.²

The technique is an important part of the treatment of proliferative diabetic retinopathy and leads to improvement or stabilisation of vision in 90% of patients.¹⁻² Vitreous and blood are cut and aspirated and membranes causing tractional detachment of the retina are removed. This may be done by segmenting the membranes or by delamination, i.e. removing the whole of the posterior hyaloid and associated fibrovascular membranes by cutting them off the surface of the retina.

In countries without screening, many people present with long-standing tractional retinal detachments of the macula. The result of diabetic vitrectomy in these eyes is not so good. In a resource-poor environment, those with a better prognosis should be prioritised.

It is worth pre-treating patients with intravitreal bevacizumab prior to vitrectomy.³ A Cochrane review of six randomised controlled trials found that pre-treatment with 1.25 mg of intravitreal bevacizumab resulted in shorter operations with less endodiathermy and intra-operative bleeding. Post-operative reabsorption of blood was significantly shorter. Final best-corrected visual acuity was significantly better.

The effect of intravitreal bevacizumab on neovascularisation is rapid. The first effects can be seen in 24 hours. The optimum time for a preoperative injection would seem to be 5–7 days before the operation.

In a proportion of patients, intravitreal bevacizumab preoperatively may lead to clearing of the vitreous haemorrhage, thus avoiding surgery.

**Treating diabetic maculopathy**

Diabetic maculopathy is a major cause of vision loss amongst patients with diabetes. Treatment includes steroids, anti-vascular endothelial growth factor (anti-VEGF), and laser.

**Steroid treatments**

In the Diabetic Retinopathy Clinical Research Network trial, intravitreal injec-
treatment of diabetic maculopathy are ranibizumab® (Lucentis) and bevacizumab® (Avastin). These trials showed a benefit with intravitreal ranibizumab and bevacizumab in patients with foveal thickening. However, intravitreal ranibizumab injections cost around US $1,200 each and the patients in this study received eight or nine injections in the first year (a cost of around US $10,000 per patient per year.) Intravitreal bevacizumab is much cheaper. We are able to offer patients an intravitreal bevacizumab injection for as little as US $25.

In practice, laser should remain the cornerstone of treating clinically significant macular oedema and the use of intravitreal injections should be tailored to the needs of individual patients.

Laser
The Early Treatment of Diabetic Retinopathy study compared macular laser with observation. There was a 50% reduction in moderate visual loss in the group that received laser (from 24% to 12%).

The recommended protocol is as follows:

1. Treat circinate exudates (Figure 6) with focal laser, blanching the retina.
2. Give PRP to anyone who has vitreous or sub-hyaloid blood (Figure 5) even if there are no visible new vessels. Treat any size area of definite neovascularisation, on the disc or elsewhere.
3. Treat patients faster. Regression of new vessels should be seen after a week or two. (Figures 8 and 9). If patients come from far away, consider admitting them to complete the laser before they are discharged. Attempt to complete the laser in one week, instead of several weeks. Treat the inferior retina first as new blood falls down and blocks the view inferiorly.
4. Make the most of each session you have. It is worth treating some patients in one session. This is particularly important if there are large neovascular (NV) formations which have an increased risk of bleeding, or if the patient is unlikely to return. Remember to avoid application of intense burns which are unnecessary to induce regression. A pan-retinal pattern of excessively intense burns can lead to choroidal effusion and angle-closure glaucoma with blindness. Treat one burn width apart, as shown in Figure 10. Oedema surrounding the burns makes them look more confluent than they are.
5. Repeat treatment. All neovascularisation should regress in two to four weeks. If it has not regressed, treat again. If bleeding occurs after laser, re-treat until NV formations have gone or maximal treatment has been given. Consider treating inside the arcades, particularly temporally.

Managing diabetic retinopathy in Africa

Case study
In our clinic, a typical patient, Mrs X, was first seen with a visual acuity of 6/9, a few macular exudates, and proliferative disease. The treatment plan followed the textbook recommendation of doing focal laser for the maculopathy first. The patient then missed two appointments and pan-retinal photocoagulation (PRP) was delayed by about two months. When PRP was finally given, the intention was to give it in the recommended multiple sessions. However, due to further missed appointments, the interval between laser sessions was over a month. This allowed fibrovascular proliferation to continue. It was six months from the time of presentation before laser was completed. By then, tractional retinal detachment involving the macula had developed and vitrectomy was required. Mrs X’s final visual acuity was counting fingers at three metres.

What are the lessons to be learned from this? How can we do better?

We audited a number of patients who had ultimately needed vitrectomy for advanced proliferative disease to find out how we could improve, and arrived at the following recommendations for laser in countries where patients may not come for regular appointments.

Recommendations
1. Warn all diabetes patients to come if they experience floaters or blur, as these symptoms suggest a vitreous haemorrhage.
2. Give PRP to anyone who has vitreous or sub-hyaloid blood (Figure 5) even if there are no visible new vessels. Treat any size area of definite neovascularisation, on the disc or elsewhere.
3. Treat patients faster. Regression of new vessels should be seen after a week or two. (Figures 8 and 9). If patients come from far away, consider admitting them to complete the laser before they are discharged. Attempt to complete the laser in one week, instead of several weeks. Treat the inferior retina first as new blood falls down and blocks the view inferiorly.
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Cataract and diabetic retinopathy

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When managing the cataract of a patient with diabetes, you should remember that cataract surgery may make diabetic retinopathy worse. Eyes with mild to moderate non-proliferative diabetic retinopathy at the time of surgery are considered less at risk. Those with severe non-proliferative and proliferative diabetic retinopathy have a higher risk of progressive disease. Clinically significant macular oedema (CSMO) present at the time of surgery is likely to progress and eyes with previously treated CSMO are at increased risk of recurrence. The risk of progression is increased if the operation is complicated by excessive manipulation, vitreous loss, or severe post-operative inflammatory reaction.

Ideally, when the cataract does not preclude laser treatment, you should achieve and maintain effective control of retinopathy and macular oedema for at least three months before surgery. The severity of the cataract sometimes prevents adequate examination or treatment of the retina in patients with diagnosed or suspected severe non-proliferative and proliferative diabetic retinopathy. In this case, you should deliver pan-retinal photocoagulation either during the procedure or in the early post-operative period. When performing intraoperative pan-retinal photocoagulation with an indirect ophthalmoscope, you should fill the anterior chamber with viscoelastic and place a corneal suture. Complete the pan-retinal photocoagulation before inserting the intraocular lens. This will provide a stable anterior chamber and optimal view, particularly if you anticipate indentation of the periphery.

If you plan to give laser treatment with a contact lens in the early post-operative period, then you should suture the corneal wound. If it is still considered hazardous to use a contact lens then effective slit lamp laser can still be applied through a non-contact 78D or 90D lens. You can also use indirect laser for pan-retinal photocoagulation.

‘You should remember that cataract surgery may make diabetic retinopathy worse’

Consider intravitreal triamcinolone or anti-VEGF at the end of surgery to reduce macular oedema and/or more advanced retinopathy, consider intravitreal triamcinolone or anti-VEGF at the end of the procedure to reduce macular oedema. Triamcinolone targets the inflammation that exacerbates the oedema. Anti-VEGFs also reduce retinal swelling and may improve visual outcomes. Intravitreal steroids may cause raised intraocular pressure and anti-VEGF agents increase the risk of retinal complications in eyes with fibrovascular proliferation. You should still apply macular laser for CSMO post-operatively.

In diabetes patients, it is very important to minimise post-operative inflammation. You should use post-operative topical non-steroidal anti-inflammatory drugs in addition to routine topical steroid preparations, particularly in those with pre-existing macular oedema.

In summary, diabetes patients with mild to moderate diabetic retinopathy and no maculopathy have a good prognosis following cataract surgery. You should treat more advanced retinopathy or maculopathy at least three months prior to surgery if possible. Whereas laser is the most recognised form of treatment, pharmacological agents play an important role in the management of these patients. It is also important to monitor high-risk patients in the post-operative period.

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