Introduction

Several complications of diabetic retinopathy need to be managed surgically. Pars plana vitrectomy (PPV) in diabetic patients has several established indications and some that are still under discussion. Vitrectomy offers relief from retinal traction, clearing of media opacities, and stabilization of the proliferation process. Vitreous hemorrhage, severe fibrovascular proliferation with traction retinal detachment, and traction-rhegmatogenous retinal detachment affecting or threatening the macula are classic indications for PPV, whereas diffuse macular edema is a nonstandard indication for this procedure. Diabetic macular edema associated with posterior hyaloid traction was added as an indication for vitrectomy. In addition, vitrectomy surgery with or without internal limiting membrane peeling has been performed in some patients with macular edema without a taut posterior hyaloid.

In cases of diffuse macular edema, vitrectomy is only indicated in cases refractory to focal laser and several intravitreal injections of triamcinolone or anti-VEGF. In cases of attached posterior hyaloid without a thickened vitreous membrane, some authors have described benefits

from vitrectomy with or without internal limiting membrane peeling. Nevertheless, this indication for vitectomy remains uncertain. Anti-VEGF or triamcinolone can be left at completion of surgery. In cases of diffuse macular edema with taut posterior hyaloid observed by ophthalmoscopy and optical coherence tomography, the benefits include opening, elevating, and removing the posterior hyaloid.

The initial description of small gauge vitrectomy, preceded its adoption by many years. The initial set of 25_G instruments developed by de Juan and Hickingobtham contained only a pneumatic vitrector, scissors, and a membrane removal instrument for use in pediatric eyes. A 23_G vitrectomy probe was introduced in 1990 by Peyman, although its intended application was limited to vitreous and retinal biopsy. Small gauge pars plana vitrectomy was popularized by Gildo Fujii who introduced a sutureless, transconjunctival, 25_G PPV system for use in a variety of surgical cases in 2002. Two years later, Dutch Ophthalmic Research Center (DORC) working with Klaus Eckardt presented the first 23_G vitrectomy system. Alcon laboratories subsequently developed a single step 23_G vitrectomy system. The exploration of yet smaller gauge

instruments continued with the introduction of a 27_G vitrectomy.

Current microincision vitrectomy surgery (MIVS) with 25_ or 23_G instrumentation has simplified the vitrectomy procedure and offers numerous potential advantages over traditional 20_G surgery including shorter operating time, reduced corneal astigmatism, diminished conjunctival scaring, less postoperative inflammation, improved patient comfort, and, in some cases, earlier visual recovery.

Currently, complex techniques are required for self-sealing 23_ and 25_G wounds. Additionally, reports of wound-sealing–related complications, such as hypotony and endophthalmitis, have surfaced as a result of increasing use of MIVS with 23_ and 25_G instrumentation.

Although the development of 27_G vitrectomy is an ongoing project and has not yet been established as a widely accepted system, the feasibility and safety of 27-G vitrectomy in selected cases have been demonstrated and confirmed. Further development and refinement of the 27-G instruments' stiffness and functionality will continue over the coming years and allow us to establish an ultra-minimally invasive surgery system for vitreoretinal diseases in the near future.

Aim of the Work

Is to review the literature regarding the role of 25 and 27 gauge vitrectomy in Diabetic retinopathy.

Chapter (1)
Diabetic Retinopathy

Definition

Diabetic retinopathy (DR) is a pathological retinal condition attributed and related to the pathogenic mechanisms of diabetes mellitus (DM) and is characterized by vascular, inflammatory and degenerative changes which can result in retinal detachment and loss of vision ***(Hendrick et al., 2015).***

Epidemiology and risk factors

1. Incidence

The incidence of DR shows great variation between studies due to the duration and location of the study and type of DM. In a 15 years study conducted in Bangladesh, the cumulative incidence of DR was 50.6% in DM type 2 patients ***(Ahmed et al., 2012).***

In a Spanish cohort including DM type 2 patients, the cumulative 4-year incidence was 8.07%, which was notably lower than the previous study ***(Salinero-Fort et al., 2013)***. In another study performed in Denmark on type 1 DM, over 16

years, the 16-year incidence of proliferative diabetic retinopathy (PDR) was only 31.0 % ***(Broe et al., 2014).***

Females show higher incidence rates of DR ***(Kajiwara et al., 2014)***. However, males show a higher trend of vision-threatening DR ***(Lin et al., 2014)***.

2. Prevalence

The prevalence of DR is strictly related to the prevalence of DM and both, unfortunately, increase. In a US study, it was estimated that 28 % of diabetics over 40 years had DR and in 4 % of cases, the disease critically threatens their vision ***(Zhang et al., 2010).*** In India, DR prevalence in a population including 6218 known diabetics was 21.7% ***(Gadkari et al., 2016)*** while in Tanzania, DR was diagnosed in 27.9% of 3187 diabetics ***(Cleland et al., 2016)*** and in Nigeria, the prevalence of DR was 32.1 % whereas prevalence of PDR was 6.4 % and diabetic macular edema 31.3 % ***(Kizor-Akaraiwe et al., 2016).***

3. Risk factors

The reported risk factors for DR include hypertension, duration of diabetes > 10 years, uncontrolled diabetes, total cholesterol ≥ 200 mg/dL and HbA1c ≥ 7%. Of these factors,

duration of type 2 DM is the most important factor ***(Liu et al., 2015).***

Pathophysiology

The hyperglycemic milieu in DR patients promotes multiple pathological mediators. These include increased levels of advanced glycated end products, enhanced oxidative stress, accumulation of polyol, and activation of protein kinase C. These mediators act synergistically to disturb cellular metabolism, biochemical signalling and growth factors secretion. These result ultimately in microvascular damage with subsequent vascular occlusion, increased capillary permeability and injury of supporting structures ***(Behl et al., 2016).***

As the disease progresses, the retinal blood vessels are finally damaged and the vascular pericytes are vanished leading to alteration of the physiological capillary exchange and leakage of endovascular products in the retina ***(Bandello et al., 2013).***

The enhanced oxidative stress and microvascular occlusion lead to retinal hypoxia, which in turn causes augmented expression of vascular endothelial growth factor **(VEGF).** VEGF is an important contributor to both vascular

leakage and promotion of new blood vessel growth. It also acts together with the existent dyslipidemia resulting in exaggerated platelet adhesiveness, erythrocyte aggregation, and fibrinolysis ***(Tarr et al., 2013).***

Classification

The classification of DR is summarized in Table-1.

Table (1): classification of DR ***(Canadian Ophthalmological Society, 2012).***

Mild nonproliferative diabetic retinopathy (NPDR) Microaneurysms
Moderate nonproliferative diabetic retinopathy Intraretinal hemorrhages, hard exudates, cotton wool spots, venous beading less than required for severe NPDR
Severe nonproliferative diabetic retinopathy Any of the following (4/2/1 rule) Extensive intraretinal hemorrhages in each of 4 quadrants Venous beading in more than 2 quadrants One intraretinal microvascular abnormality (IRMA)
Proliferative diabetic retinopathy (PDR) Any of the following Neovascularization Vitreous/preretinal hemorrhage

Diagnosis

a. Symptoms

Essentially, DR is symptomless, especially if only one eye is affected. Visual Impairment from DR can be due to diabetic macular edema (DME) and PDR ***(Nentwich and Ulbig, 2015).***

b. Signs

DR is not the sole ocular complication of diabetes. Ocular manifestations of diabetes include high risk of papillopathy, cataract, glaucoma, and ocular surface diseases, which can affect vision in various degrees. Coexistence of two or more complications in not uncommon ***(Sayin et al., 2015; Misra et al., 2016).***

Diabetic macular edema

Clinically, DME appears as blunting of the foveal contour, hard exudates, and visible retinal thickening ***(Gundogan et al., 2016).*** Clinically significant macular edema (CSME) exists if any of the following criteria are met:

- Any retinal thickening within 500 μm of the foveal center. (Center Involving ME)

- Hard exudates within 500 μm of the foveal center that are associated with adjacent retinal thickening (which may lie more than 500 μm from the foveal center). (Non-Center Involving ME)
- An area of retinal thickening at least 1 disc area in size, any part of which is located within 1 disc area of the foveal center. (Non- Center involving ME) (Early Treatment Diabetic Retinopathy Study Research Group 1985-1987)

Proliferative diabetic retinopathy

Advancement from NPDR to PDR is marked by neovascularization (above the ILM), which has a poor visual prognosis. Loss of vision can occur in advanced cases due to vitreous hemorrhage and tractional retinal detachment ***(Gündüz and Bakri, 2007).***

Vitreous hemorrhage (VH)

When retinal neovascularization extends to the vitreous cavity, vessels can easily and spontaneously, shear leaking blood into the vitreous, which manifests as black debris, shadows, and floaters in the vision. Depending on its density, VH can affect visual acuity at levels varying from mild impairment to inability to see movement. Fortunately, VH

can be managed surgically through PPV if spontaneous resolution within 2 weeks is not expected ***(El Annan and Carvounis, 2014).***

Tractional retinal detachment (TRD)

Neovascularization in addition to associated fibrous and glial support tissue form a fibrovascular proliferation with contractile properties. When this proliferation has enough force, it can cause retinal detachment, which can lead to irreversible vision loss unless successful surgical repair is enacted within a reasonable timeframe ***(Agarwal et al., 2015).***

Ophthalmoscopic findings

Ophthalmoscopic features of DR are summarized in table 2.

Table (2): Features of diabetic retinopathy

Microaneurysms	small circular red lesions in the retina; represents saccular vascular weakness and typical focal point of vascular leakage, represents early signs of DR (Fig. 1)
Intraretinal hemorrhages	larger, more irregular red lesions in the retina; not intrinsically visually threatening, generally resolve within 3 to 4 months (Fig. 2)
Hard exudates	yellow irregular shaped lesions; represent intraretinal lipids and protein deposition. When accompanied by retinal thickening, represent feature of DME(Fig. 3)
Cotton-wool spots	superficial feather-bordered white lesions; represent nerve fiber layer infarctions from capillary occlusion (Fig. 4)
Intraretinal microvascular abnormalities:	alterations to blood vessel from capillary closure that lead to visible vascular remodeling
Venous beading	dilated, tortuous, and irregular in caliber veins adjacent to capillary nonperfusion
Macular edema	breakdown of the blood-retinal barrier promotes leakage of plasma from bloodstream into the retina causing swelling; can occur early in DR development, often presents alongside hard exudates and microaneurysms (Fig. 3)
Neovascularization	fine, lacy abnormal proliferation of new blood vessels; can extend into the vitreous cavity and bleed into the vitreous (Fig. 5)
Vitreous hemorrhage	bleeding into the vitreous cavity (Fig. 5)
Tractional retinal detachment	contraction of fibrous proliferation associated with neovascularization can separate the retina from its anatomic position
Neovascular glaucoma	new blood vessel growth into the Angl occludes it, driving up intraocular pressure

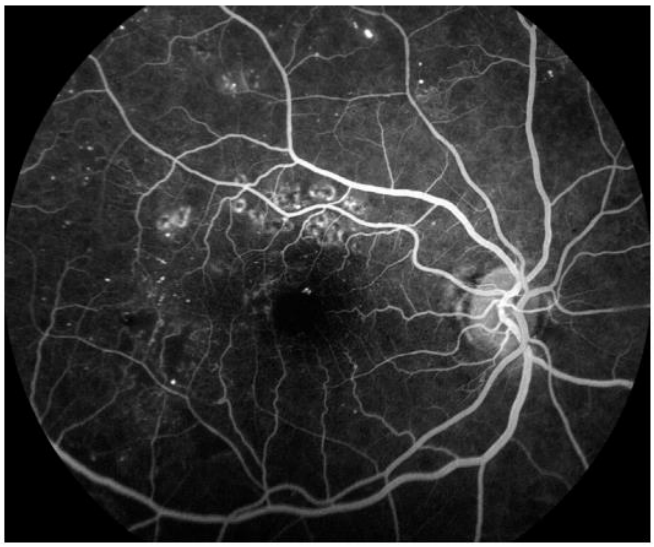

Figure (1): Fluorescein angiogram-right eye-transit phase. Many light-bulb microaneurysms appear hyperfluorescent in the macula in conjunction with laser burns seen in the superior macula. ***(Hendrick et al., 2015).***

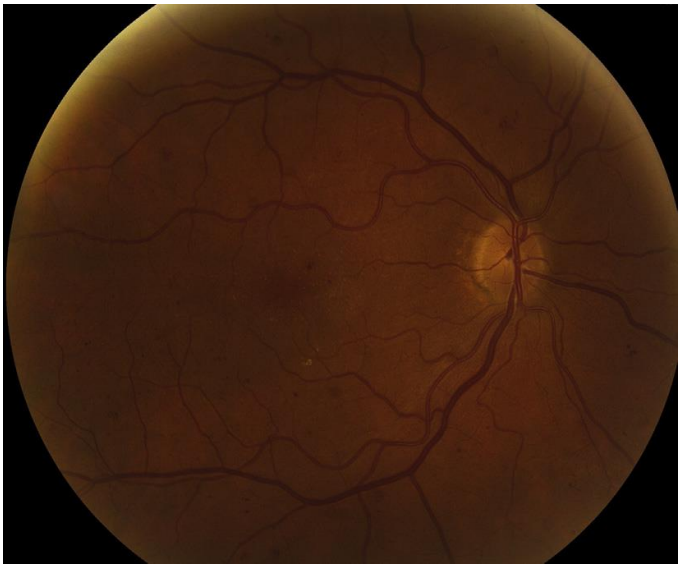

Figure (2): Fundus photograph-right eye showing multiple punctate circular microaneurysms. In addition, a large dot blot hemorrhage can be seen beside the inferotemporal arcade. ***(Hendrick et al., 2015).***

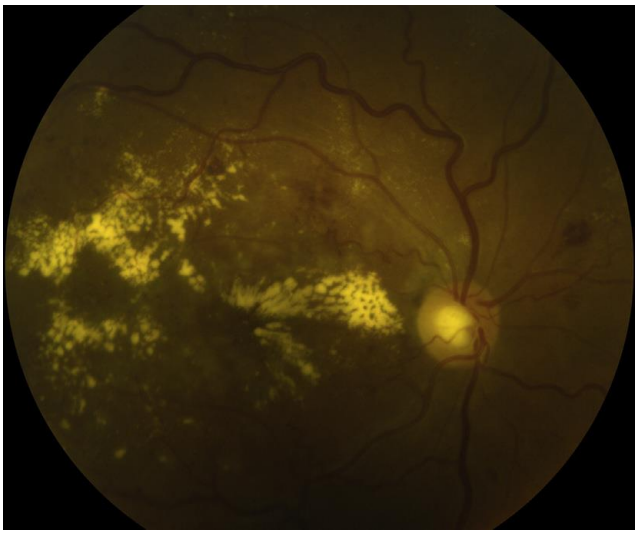

Figure (3): Fundus photograph-right eye. Massive intraretinal lipid exudates and thickening within the macula from DME. ***(Hendrick et al., 2015).***

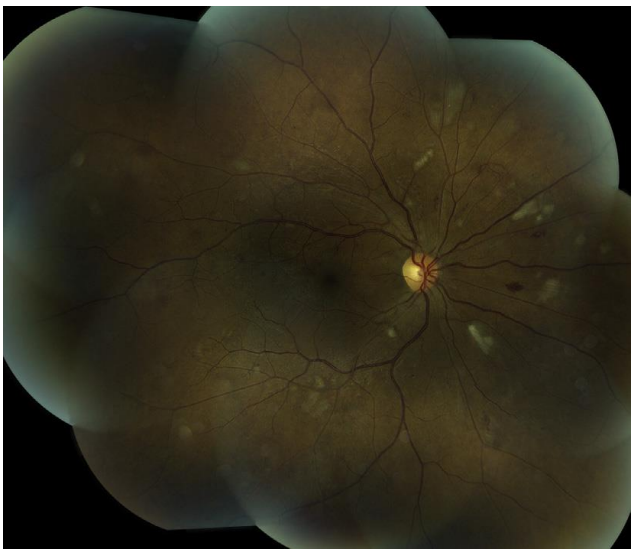

Figure (4): Montage fundus photograph-right eye. Fluffy white lesions scattered in superficial retina surround the optic nerve. An intraretinal microvascular abnormality can be found in the superonasal fundus. ***(Hendrick et al., 2015).***

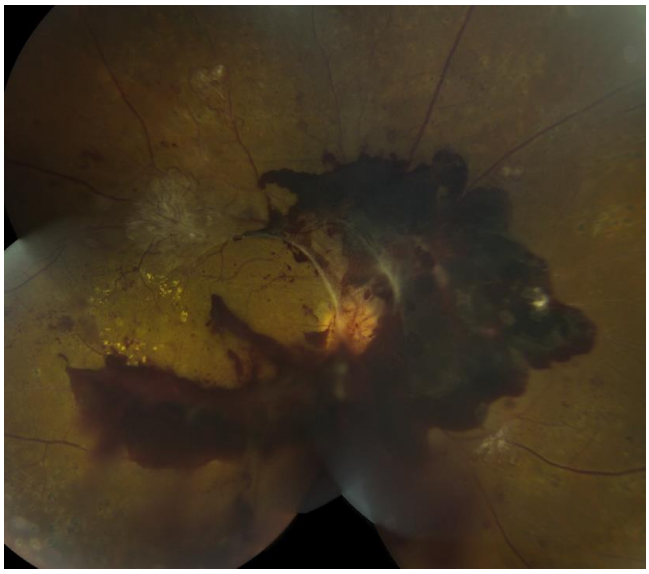

Figure (5): Montage fundus photograph-right eye. Vitreous hemorrhage and nerve neovascularization with proliferative DR. ***(Hendrick et al., 2015)***

Investigations

A. Diabetic monitoring

Continuous diabetic control monitoring using hemoglobin A1c (HbA1c) is essential for follow-up of patients especially those with PDR. In parallel, other diabetic complications should thoroughly be watched including renal functions, serum lipids and nerve functions ***(Hendrick et al., 2015).***