

Macular Hole

Yog Raj Sharma, Rajeev Sudan, Amit Gaur, Raja Rami Reddy



A macular hole is a full thickness defect or tear of the neurosensory layers of retina involving the anatomic fovea of the eye. The majority of macular holes are primary idiopathic macular holes. Secondary macular holes may occur in association with a variety of conditions including blunt trauma, high myopia optic disc coloboma, optic nerve pit, long standing retinal detachment with long standing cystoid macular edema resulting from veno-occlusive diseases or diabetic retinopathy, Best's disease, adult vitelli form macular degeneration, retinal arterio venous communication, choroidal neovascularizations, topical pilocarpine, solar eclipse macular burns, and may be found after successful retinal reattachment surgery by scleral buckling or pneumatic retinopathy.

Historical Perspective and Etiological theories

Herman Knapp in 1869 described the first case of macular hole, in a patient who had sustained a severe contusion and in whom an initial diagnosis of a macular hemorrhage was made(1). Two years later Noyes made the first accurate and detailed ophthalmoscopic description of a macular hole that was again secondary to blunt trauma(2). Nevertheless the entity of macular hole was not widely recognized until the turn of the century. Trauma was originally thought to be the primary, if not the sole, etiological cause with traumatic macular holes accounting for half of all cases of macular holes in the beginning of this century(3). Hole formation was explained by rupture of fovea from mechanical energy created by vitreous fluid waves and counter coup macular necrosis or laceration(4). It was also recognised that blunt trauma

was sometimes followed by cystoid macular edema which ruptured later producing macular holes(5).

Soon non traumatic cases of macular holes began to be reported(6). Coats was among the first to recognize that macular cystoid degeneration was often not related to trauma and supported cystic degeneration theory of macular hole(4). Intraretinal cystic changes which coalesced creating full thickness macular hole could be caused by trauma as well as other atraumatic mechanisms. Vascular theory of pathogenesis was the other major atraumatic theory of macular hole formation which became popular. It was believed that aging and other changes of the retinal vasculature led to cystoid retinal degeneration and subsequent macular hole formation(7). Lister in 1924 was the first of many to implicate anteroposterior vitreous forces in the pathogenesis of macular holes(5). Various other proponents of vitreous theory extended this hypothesis by emphasizing that the process of posterior vitreous detachment (PVD) was the critical event in the pathogenesis of a macular hole causing avulsion of inner retinal layers(8). As PVD is a common event in the age group of those at greatest risk for idiopathic macular hole formation, it is difficult to ascribe a causal relationship between these two events.

Morgan and Schatz in 1986 proposed a mechanism of macular hole formation that they described as involitional macular thinning, which incorporates vitreous, vascular and cystic degeneration theories(9).

In 1988, Gass and Johnson described a classification scheme for idiopathic macular holes which incorporated

From the Department of Ophthalmology, Dr. Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi.

Correspondence to: Dr. Y.R. Sharma, Additional Professor of Ophthalmology, AIIMS, New Delhi.



their ideas of the pathogenesis of these lesions. They concluded that attached vitreous was critical to macular hole formation. As the stages of development of a macular hole caused loss of normal foveal anatomic depression but no elevation of tissue above the parafoveal retina, they hypothesized that focal shrinkage of the prefoveal vitreous cortex and tangential retinal traction are responsible for macular hole formation.

Pathogenesis and Clinical Staging of Macular Hole Formation

Clinical stages of idiopathic macular holes were originally described in a retrospective series by Gass and Johnson and were updated in a subsequent prospective series (10,11,12).

Stage IA (Impending hole)

Biomicroscopic finding: A yellow spot, 100-200H in diameter, centered on the foveola. Associated loss of foveal depression (hence foveal reflection) occurs. No vitreo foveolar separation.

Anatomic Interpretation: Spontaneous tangential traction of the external part of the prefoveal cortical vitreous causes serous detachment of foveolar retina creating an intraretinal yellow spot. The yellow color results from intraretinal xanthophyll pigment. This finding is not pathognomonic of macular hole.

Stage IB (Impending or occult hole)

Biomicroscopic findings: A yellow ring, 200-300H in diameter, centered on the foveola, associated loss of foveolar depression with no vitreo foveolar separation.

Anatomic interpretation: After the serous foveolar detachment the foveal retina detaches and elevates to the level of the surrounding perifoveal retina, elongating the foveal retina around the umbo (impending hole). This is followed by centrifugal displacement of the retinal photoreceptors, xanthophyll and radiating nerve fibres leading to a dehiscence of the deeper retinal layer at the umbo. As the overlying internal limiting membranes, horizontal processes of Muller cells, and prefoveal vitreous condensation remains intact, the dehiscence is

not detected by biomicroscopy (occult hole). The yellow ring appears at edge of the centrifugally displaced retinal receptors. This finding appears to be specific to macular hole formation.

Stage 2

Biomicroscopic finding: Small full thickness retinal defect (<400H) which may be eccentric, oval, crescentic or horse-shoe shaped at inner of yellow ring or a central round retinal defect with rim of elevated retina. Hole may be present with or without a prefoveal opacity.

Anatomic interpretation: A hole (tear) occurs in the contracted prefoveal vitreous condensation bridging the occult retinal hole, so the retinal defect is identifiable biomicroscopically as stage 2 hole. Spontaneous vitreofoveal separation may occur creating a semi-transparent prefoveal opacity (pseudopericulum) that is often larger than the underlying foveolar hole. There is no loss of foveolar retina and no posterior vitreous detachment from optic disc and macula.

Stage 3

Biomicroscopic finding: Full developed, central round, 400H diameter hole, with rim of elevated retina. A prefoveal opacity may or may not be associated.

Anatomic interpretation: A full thickness hole with no posterior vitreous detachment from optic disc and macula, vitreofoveal separation may form a prefoveal opacity (pseudopericulum)

Stage 4

Biomicroscopic finding: Full thickness hole rim of elevated retina and Weiss Ring. A prefoveal opacity may or may not be present.

Anatomic interpretation: A full thickness hole with complete posterior vitreous detachment from optic disc and macula.

Based on their findings, Gass concluded that as the fovea was never elevated anterior to the plane of the retina, antero-posterior traction with PVD was not the mechanism for macular hole formation. They proposed that in the pathogenesis of idiopathic macular hole,

shrinkage of attached posterior cortical vitreous occurs that generates tangential traction that is transmitted to the foveal retina. The biophysical mechanism for this shrinkage of the posterior cortical vitreous is not known. Guyer and Green proposed three possible mechanisms for generating tangential traction. Fluid movements, cellular remodelling of the cortical vitreous, and cellular proliferation on the inner surface of the cortical vitreous(13). Madreperla and Mc Cuen have suggested a concept of macular hole formation. Initially foveolar detachment is caused by traction directed at fovea by detachment of para foveal cortical vitreous which is attached at fovea. Continued traction from detached para foveal cortical vitreous leads to foveolar dehiscence. Swelling of foveal retina occurs with retraction of foveal hole edges(enlargement of macular hole). Concurrently glial cells grow from edges of retinal defect along posterior face of cortical vitreous. Continued traction from detached para foveal cortical vitreous leads to break between glial cells and macular hole edge. This dehiscence progresses around the entire circumference of the hole resulting in formation of a pseudo operculum overlying the full thickness retinal defect and attached to posterior cortical vitreous(14).

Histopathology of Macular Holes

Histopathologic series of post mortem cases of macular hole reported by Frangieh et al and Gyer et al have provided information regarding pathogenesis and rationale for management of macular holes(15,16)

Full thickness macular holes are characterized by absence of all retinal layers in an area usually centred at the fovea. They are usually surrounded by rounded retinal edges and a cuff of detached neurosensory retina with subretinal fluid. Lamellar macular holes are characterized by partial loss of inner neuro sensory retinal layers with no cuff of detached retina. Cystoid macular edema (79%) and epiretinal membranes (68%) are the most common associated features. RPE changes are not uncommon. Photoreceptor adjacent to the hole are

degenerated variably in long standing cases. A thin layer of epiretinal tissue is seen overlying the macula in stage 1, 2 and 3 holes and has been found to be posterior cortical vitreous. This finding is consistent with Gass's theory that prefoveal cortical vitreous plays a role in pathogenesis of macular holes. Postmortem studies on patients having had macular hole surgery have also provided unique information. The healed macular hole appears as a defect in the fovea which is occupied by Muller cell processes and fibrous astrocytes. Photoreceptors adjacent to the healed hole appear normal usually. No RPE abnormalities or CME were found. The size of the healed hole is found to be much smaller than that noted preoperatively. Madreperla and colleagues suggested that surgical relief of tangential traction and flattening of the edematous edges of the hole allow the setting of the macular hole and reapproximation of the edges. Any residual defect is sealed by glial cells (fibrous astrocytes and Muller cells). The presence of normal photoreceptors around the hole and absence of CME and retinal detachment accounts for the observed improvement in vision after holes have been successfully treated(17).

The prefoveal vitreous opacity present in many eyes with macular hole was initially termed an operculum and was believed to represent retinal tissue that at one time occupied the hole. Histopathologic feature of this tissue obtained during vitrectomy has been studied using transmission electron microscopy(18). The tissue were composed of Muller cells and fibrous astrocytes, with a thin layer of cortical vitreous lining the internal surface. Importantly there were no photoreceptors or neural tissue as would be expected if the tissue represented a piece of foveolar retina. It was concluded that the pre hole opacity did not represent retinal tissue but rather avulsed glial tissue possibly involved in an attempt to heal the hole and should be referred to as a pseudo operculum. It has also been suggested that glial cells present in these tissue may be agents in the primary pathogenesis of macular holes rather than simply elements of a reparative process.

Clinical Characteristics and Epidemiology of Macular Holes (19,20,21)

Idiopathic macular holes are most common accounting for 83% of cases, 15% cases are due to trauma (accidental or surgical) and rest are secondary macular holes associated with other conditions mentioned above. The peak incidence of idiopathic macular hole development is in the seventh decade of life. A female preponderance is observed(80%).

Symptoms

The majority of idiopathic macular holes are asymptomatic in the early stages. Patients who are symptomatic with macular holes complain of blurred central vision or a central scotoma and metamorphopsia. Usually they notice only a mild loss of vision particularly apparent when reading or driving. Symptoms develop relatively gradually and it may be some time before they cover one eye and detect that the central decrease in acuity is monocular. Some patients may remain entirely asymptomatic and the hole is diagnosed only on routine ophthalmologic examination or by the optometrists who are alerted to the condition by the poor visual acuity. The visual acuity of stage 1 hole is often as good as 6/9 or 6/12. Once full thickness hole is identifiable (stage 2 onwards) vision varies between 6/18 to 3/60. Patients with recent, small eccentric stage 2 hole may retain excellent visual acuity (6/9-6/12). As a rule of thumb, a full thickness macular hole does not maintain a visual acuity 6/18 or better for more than 3 months. Metamorphopsia is caused by elevation of neuro sensory retina around the hole.

Clinical examination

The detection of macular hole is best achieved by slit lamp biomicroscopy using a contact Iron contract/non lens. The Gass classification system is used most widely to describe the clinical appearance and evaluation of macular holes. In stage 1A (impending hole) a yellow spot is seen, a yellow ring is noted in stage 1B (impending or occult hole) Stage 2 is diagnosed when a full thickness defect <400 m in diameter is first noted clinically, usually

near the inner edge of the yellow ring. Stage 2 holes can be centric and eccentric. Small stage 2 holes can be difficult to see and use of narrow high intensity slit beam and high magnification can aid their detection. In stage 3 & 4 holes, a round excavated lesion (>400m) is seen interrupting the beam of slit lamp. In majority of patients, an opacity (pseudooperculum) can be seen suspended over the hole. Often there is a surrounding cuff of edema and subretinal fluid. Histopathologic studies show that only a very small amount of actual retinal detachment occurs and most of the perceived cuff at the border of the holes is due to surrounding cystic edema of retina. Retinal pigment epithelium (RPE) at base of hole appears intact and normal in acute holes, but chronic changes include pigmentary atrophy and hyperplasia leading to a granular appearance. Characteristic yellow refractile dot like deposits may be seen at the base of hole(42% of cases), these may represent lipofuscin laden macrophages or nodular proliferations of RPE overlying eosinophilic material. Epiretinal membrane formation may be present in some cases. Weiss Ring (complete PVD) is seen in stage 4. Macular holes may vary in size depending in part on their duration. Average hole measure 500-800H

Ancillary Tests

Although clinical examination remains the gold standard for diagnosis, these tests assist in making a diagnosis of macular hole and in differentiation from other pseudo hole conditions.

a) Fluorescein Angiography: This may be a useful adjunct to biomicroscopy. In stage 1 faint hyper fluorescence or more typically no abnormality at all is seen on fluorescein angiography. In stage 2 holes, fluorescein angiography may reveal a round area of window defect or may remain normal. Stage 3 and 4 holes typically produce a window defect with early transmission of fluorescence in phase with choroidal filling through the central retinal defect. No late leakage or accumulation of dye is seen. In some cases particularly those involving very small holes or holes accompanied by RPE

abnormalities, distinguishing the characteristic hallmark window defect may be difficult.

b) **Watzke Allen Test:** This is performed by placing a thin vertical slit lamp beam directly on hole during contact lens biomicroscopic examination. Patient with positive Watzke Allen sign will perceive an interruption in the light beam. A normal appearing or only narrowed beam is a negative result. This is a highly sensitive and specific clinical test distinguishing full thickness macular holes from pseudo-holes. If negative with vertical beam, a horizontal beam can be tried. Another useful maneuver is moving the slit lamp beam slowly across the macula and asking the patient whether at any time the beam is clotted or broken.

c) **Laser Microperimetry:** The aiming beam on a laser delivery system is also a good test for assessing the presence or absence of a full thickness macular hole. The patient is seated at the laser with contact lens in place. A 50 Paiming beam is used to test central areas of retina focally for sensitivity. The inability of the patient to perceive the spot in the area of presumed macular hole (absolute scotoma) confirms the lack of retinal tissue in that location (full thickness hole).

d) **Optical Coherence Tomography(OCT):** This is a new diagnostic imaging technique for high resolution imaging of the retina(22). Cross sectional images of retina can be obtained with 10 longitudinal resolution. OCT is performed with patient sitting at slit lamp into which a 78D lens has been mounted. A superluminescent diode laser produces a probe beam of wavelength 840 units (infrared) that is focussed in the retina. A pair of galvanometrically driven ortho gonial scanning mirror scans the beam within the eye and area of retina scanned can be visualised with an infra red camera. Cross sectional images of retina are displaced in colours corresponding to regions of high relative optical reflectivity (red and white) or low reflectivity (blue to black). High resolution tomographic images provided by OCT can help differentiate true macular holes from pseudo holes and lamellar holes.

e) Scanning laser ophthalmoscope and

f) Retinal thickness analyzer also have been used to differentiate between macular holes and mimicking conditions.

Differential Diagnosis

Macular holes are often misdiagnosed. Careful biomicroscopic examination with a contact lens is required to make an accurate diagnosis. Various ancillary tests mentioned above help in differentiation. A true full thickness macular hole has a distinct and circular margin, often with a surrounding cuff of subretinal fluid and an overlying pseudo-operculum. Vision is usually 6/18 or worse while macular pseudo holes fare better.

a) **Hole in epiretinal (epimacular membrane):** Most commonly confused lesion is an epiretinal membrane that has a hole, contraction or circumlinear edge in or near the fovea. Contact lens biomicroscopy shows the membrane itself with contracture and macular puckering with normal retina beneath the membrane. No cuff of subretinal fluid and retinal edema is found around the hole and fluorescein angiography shows no window defect. It is important to note that epiretinal membranes may be found in association with macular holes as well, so presence of one does not rule out the diagnosis of macular hole.

b) **Age related macular degeneration (ARMD):** Geographic atrophy of RPE and overlying retina may, when sharply demarcated circular and central, mimic the appearance of macular hole.

c) **Cystoid macular edema(CME):** When a large central cyst is present it may simulate the presence of full thickness macular hole. Other ocular conditions associated with CME (recent intraocular surgery, ocular inflammatory condition etc.) and fluorescein angiography help in differentiation.

d) **Lamellar macular holes:** These are partial thickness defect of macular retina most often the result of aborted macular hole formation or seen in cases of chronic CME when the thin inner layer of the cyst breaks. A

pseudo-operculum may be observed overlying the lamellar macular hole contributing to misdiagnosis. Neither cuff of retinal edema or subretinal fluid nor central window defect on fluorescein angiography are demonstrated. Borders of lamellar hole are less slowly defined and have more sloping edges.

e) Subfoveal choroidal neovascularization with a foveal cyst and intra retinal edema may mimic a macular hole.

f) Vitreo macular traction with a cystic fovea may also masquerade as a macular hole.

g) Various conditions that may be misdiagnosed as stage 1 macular hole (impending hole) include ARMD with a large central drusen, central serous retinopathy, cystoid macular edema, vitreomacular traction syndrome or a foveal yellow lesion associated with solar retinopathy.

Risk factors for idiopathic macular hole

The eye disease case control study group (EDCCS) reported on the demographic and risk factors for idiopathic macular hole comparing 198 subjects with macular hole with 1023 matched controls. 72% of subjects with macular hole were female. Only 3% of subject were less than 55 years of age. In the final multivariate logistic regression model that included all cases, higher fibrinogen levels and history of glaucoma were the only significant risk factors. In women, current users of exogenous estrogen had reduced risk. Other risk factor like cardiovascular disease, hypertension, history of hysterectomy, total protein, serum beta carotene, which have been suggested as risk factors in previous studies were not found to be associated significantly as risk factor for macular hole in the EDCCS.

Risk to the fellow eye

This is important point for consideration as patients with a unilateral macular hole will be concerned about the prognosis for their fellow eye. Risk to the fellow eye also needs to be considered when surgical treatment of full thickness macular hole is planned.

The vast majority of fellow eyes will not develop a macular hole, but there is definite incidence of bilaterality.

In a follow up study to the EDCCS, rate of development of macular hole in the fellow eye was 4.3-7.1% on 3-6 years of follow up(23). Other studies have reported risk of fellow eye involvement to be from 3-22%(24). The risk of development is high (40%), if the fellow eyes showed premacular hole change (Stage 1 lesions), while normal fellow eyes have a very low incidence (0.2%) particularly if there is a pre-existent posterior vitreous detachment.

Natural History of Macular Holes

Natural history of small full thickness macular hole is one of hole enlargement accompanied by deterioration of visual acuity.

Stage 1 lesions

Vitrectomy for Prevention of Macular Hole Study Group, a multicenter, randomized, controlled clinical trial was performed to better understand the natural history of early stages of macular hole (25). Forty percent of patients with stage 1 lesion progress to a full thickness macular hole over a 2 year follow up period while 60% of stage 1 lesions abort macular hole formation. Resolution of stage 1 lesion is accompanied by vitreofoveal separation. Resolved fovea may appear normal or may show a lamellar macular hole. Lamellar macular holes do not progress to macular holes (12). Posterior vitreous detachment confers protection from macular hole evolution (24). Eyes with stage 1 macular hole and best corrected visual acuity between 6/18-6/24 had a 66% rate of progression to full thickness macular hole, while eyes with 6/6-6/12 had a 30% risk of progression (26).

Stage 2 lesions

Majority of stage 2 holes demonstrate progression to stage 3 and 4 macular holes with subsequent loss of vision usually within 6 months. Hikichi reported 96% of stage 2 lesion progress to stage 3 and 4 lesions, in 85% the hole enlarges, visual acuity loss of 2 or more snellen lines occur in 71% of eyes with no eyes demonstrating resolution. Median follow up period of 4 years(27).

Stage 3 and 4 macular holes

The frequency of hole enlargement and visual deterioration is less with stage 3 and 4 lesions. Hikichi reported 55% of stage 3 lesion and 16% of stage 4 lesion, undergo macular hole enlargement during median follow up of 3 year period and visual acuity loss of 2 or more snellen lines occur in 29% of eyes with stage 3 lesion and 13% with stage 4 lesion. Progressive visual deterioration in stage 3 and 4 holes is due to increasing cuff of subretinal fluid, cystoid retinal changes and photoreceptor atrophy. 5-12% of stage 3 or 4 lesions may spontaneously flatten with improvement in visual acuity (16).

Management of macular hole : Historical Background

Until recently majority of patients with macular hole were considered untreatable with patient usually becoming legally blind in the affected eye. Surgeons focussed their attention on macular hole only if retinal detachments were associated. Surgery involved scleral buckling techniques with subretinal fluid drainage and light laser photocoagulation to flatten a macular hole. Other variations included Y shaped plombs, armed silicone implants, diathermy, cryotherapy, silicone oil or intravitreal gas injection without vitrectomy (28).

Vitrectomy with gas tamponade to achieve retinal reattachment in eye with large retinal detachment and macular holes was reported in 1982 (29). Bidwell et al reported spontaneous recovery of excellent vision (6/6) and disappearance of the macular hole in one eye and retinal reattachment with disappearance of the hole and 6/6 vision after vitrectomy and gas tamponade in one eye(30). In 1988 Gass introduced the concept of tangential vitreous traction on the posterior pole in macular holes and a classification and hypothesis for their pathogenesis(10,11). Kelly and Wendel are to be credited for the introduction and developments of vitreous surgery for full thickness macular holes. They hypothesized that vision might stabilize or improve if it were possible to surgically relieve the tangential traction, reduce the cystic changes and reattach the cuff of detached retina

surrounding a macular hole using traditional vitrectomy techniques. The pilot surgical series was published in 1991 and was updated in 1993(31,32). After this extraordinary report and remarkable success in improving vision by sealing full thickness macular holes, interest was renewed in this order which was previously considered untreatable. There was quick acceptance by many vitreous surgeons of the technique reported by Kelly and Wendel and results have been duplicated by other investigators around the world. The surgical techniques have been gradually improving along with improvement in visual results.

Surgical techniques for full thickness holes

Indications for surgical intervention are vision loss and the presence of a full thickness retinal break. The surgical objectives are to relieve all vitreomacular traction and to affect retinal tamponade. Tangential traction is released by identification and removal of the cortical vitreous and by removal of fine epiretinal membrane (ERMs) surrounding the hole. Tamponade is usually provided by total gas fluid exchange and strict post operative prone positioning.

A standard three port pars plana vitrectomy is performed to remove anterior and middle vitreous. Then a critical surgical step is the technique of induction of a complete posterior vitreous detachment (PVD). Various surgical techniques have been described including use of tapered extrusion (suction) needle, use of microvitreo-retinal blade to incise the posterior hyaloid at optic disc margin.

But the easiest and safest is the use of soft tipped silicone cannula. Using active suction (150-250mmHg), the cannula is swept gently over the retinal surfaces near the major vascular arcades, around the optic nerve or temporal to macula. The area around the macular hole is avoided as the cuff of detached retina is mobile and easily incarcerates into the port. Engagement of cortical vitreous results in flexion of the silicone tip ("fish strike" sign). The tip of cannula should be kept 1 mm away from retinal surface. As long as vitreous cortex is present this maneuver is safe as vitreous plugs the port preventing retinal incarceration. Care should be taken



if intraoperatively or preoperatively PVD has occurred (Stage 4 hole), as the retina can be aspirated into the port and torn. As the cortical vitreous can be difficult to identify, use of autologous blood to stain this tissue has been reported. Once the surgeon becomes familiar with identifying the vitreous cortex, a faster and easier method is suggested in which the vitreous cutter set on "suction only" is directed posteriorly and gently swept over the retina till cortical vitreous fibres are seen streaming into the port.

Once vitreous is engaged, a PVD is created with persistent, gentle traction as the tip of cannula is moved over retinal surface to the posterior equatorial zone. Once elevated the cortical vitreous is seen as a thickened translucent sheet. A ring of peripapillary vitreous (Weiss's ring) and a pseudo-operculum can be detected usually. These are removed with the vitreous cutter.

Preoperative examination made to detect the extent and location of ERMs help in their intraoperative identification and surgical removal. ERMs associated with macular holes are finer more friable, and more tightly adherent to the retina. A bent MVR blade is used to create an edge and then elevated with a membrane pick. The free edge is grasped with intraocular tissue forceps and stripped.

After completing the vitrectomy, a careful indirect ophthalmoscopic examination of the peripheral retina for iatrogenic retina tear is made. A total air-fluid exchange is performed. Waiting for a few minutes will allow residual intraocular fluid to collect posteriorly which is then removed to completely dehydrate the vitreous cavity. Once all the fluid has been removed the residual fluid in the base of the macular hole may be aspirated using a 33 G metal tapered tip aspiration needle, taking care to avoid touching the retinal pigment epithelium. This step is not attempted in stage 2 holes to avoid inadvertent progression to stage 3.

A non expansile concentration of long acting gas (20% SF₆, 14% C₃F₈) is exchanged for the air. In cases where surgery is performed under general anaesthesia, it is important to stop nitrous oxide administration 30 minutes before gas air exchange.

Post operatively 24 hours a day strict prone positioning for 1 week is mandatory to ensure success. An alternative approach in case where this is not possible is use of silicone oil for tamponade without prone positioning.

Results

Anatomic success in macular hole surgery is defined as attachment of the previously elevated cuff of retina surrounding the macular hole to the subjacent RPE. This is usually associated with a decrease in size of hole with the edges appearing to have slid together and becoming imperceptible in some cases. In every anatomically successful case, the cystic retinal changes around the edges of the hole resolve. These clinical observations have been confirmed histopathologically (17). It has been suggested that the surgical relief of tangential traction and flattening of the edematous edges of the hole allow settling of the macular hole and reapproximation of the edges. Any residual defect is then sealed by glial cells (fibrous astrocytes and Muller cells). The presence of normal photoreceptors around the surgically treated hole, absence of CME and retinal detachment and the fact that there is no actual loss of retinal tissue in macular hole accounts for the observed improvement in vision after holes have been successfully treated. Besides closure of macular hole and visual improvement after surgery, other changes observed are resolution of central hyperfluorescence (window defect) on fluorescein angiography and absence of absolute scotoma detected by preoperative microperimetry.

In the landmark pilot series of 20 cases presented by Kelly and Wendel, overall results were of 58% anatomic success rate and visual improvement of two or more lines in 42% of eyes (31). Later in a larger series of 170 consecutive cases of macular hole surgery they reported improved over all results to 73% anatomic success and 55% patients improving two or more lines of visual acuity (32). Various subsequent surgical series (33-35) confirmed the potential role of vitreous surgery to close full thickness

macular holes with possible recovery of central visual function with increasing reported success rates and visual acuity recovery rates. A series of surgery for stage 2 macular holes in 1994 demonstrated that 61% improved visual acuity, 27% remained stable and 12% progressed to a stage 3 macular hole with worse vision (36). As most of these series were uncontrolled, Freeman organised the Vitrectomy for Macular Hole Study Group which investigated the natural history of full thickness macular holes and role of vitrectomy surgery versus observation for full thickness macular holes in a prospective, randomized controlled clinical trial (37). In the Early Full Thickness Macular Hole Study, stage 2 macular holes were included (38). At 12 months, progression from stage 2 to a stage 3 or 4 macular hole was significantly less frequent in the surgery group (20%) than in the observation group (71%). Visual function assessment by word reading and PAM was significantly better in surgery group than in observation group at 12 month follow up, but no statistically significant difference between the two groups was seen in the ETDRS acuity or contrast sensitivity assessments. This may be related to the high rate of development of nuclear sclerosis after vitrectomy. The Fully Developed Full Thickness Macular Hole Study analysed stage 3 and 4 holes(39). At 6 month follow up vitreous surgery resulted in significant increase in macular hole closure (69%) and significantly better vision on ETDRS vision testing than in observed eyes. The randomized controlled Vitrectomy Macular Hole Study confirmed the ability of vitreous surgery to close macular holes, thus providing support for the finding of the previously published non-randomized studies. With refinement in surgical techniques success rate is improving in most centres with success rate of 85-94% for anatomical closure and 50-84% improving at least two lines of acuity or more (40).

Role of Pharmacologic Adjuvants in Macular Hole Surgery

The extremely encouraging results of macular hole surgery prompted investigators to attempt to improve the

anatomic and visual success rates by refining various stages of the surgical techniques. Histopathologic studies have demonstrated that with macular hole resolution, either spontaneously or after successful macular hole surgery, the edges are reapproximated, and the residual defect filled with fibroglial cells(17). Surgical rationale for using adjunctive therapy regimens is the stimulation of fibroglial proliferation to close the hole, avoiding trauma to adjacent functional retinal elements. Various adjuvants which have been used are biological tissue adhesive, transforming growth factor-beta₂ (TGF-β₂) autologous serum, autologous platelet concentrate.

Biological tissue adhesive, a commercially available product composed of bovine thrombin and pooled human fibrinogen, was the first adjunctive therapy reported(41). The clinical results were encouraging and subsequently various investigators have used the strategy of thrombin with a fibrinogen containing activator, such as autologous plasma or cryo precipitate derived from autologous serum(42,43). As there was failure to randomize and lack of controls in these studies, the conclusion on to the efficacy of these agents are limited. Besides, there is a report of intraretinal hemorrhage in 19% and hypopyon in 8% of patients undergoing treatment with bovine thrombin (44).

TGF β₂ stimulates collagen and glycoprotein synthesis and induces cellular proliferation and migration. A prospective pilot study of 60 eyes in which bovine derived TGF β₂ was used showed very encouraging results. Anatomic closure was induced in all the 23 patients receiving at least 330 hg of bovine derived TGF-β₂, with visual acuity improving at least two lines in 61% of cases(45). A subsequent prospective randomised trial of 90 patients confirmed the efficacy of bovine derived TGF-β₂ when compared with a placebo(46). However, because bovine derived TGF-β₂ was too costly for large scale production, recombinant TGF-β₂ was developed.

Unfortunately, the results of phase III, prospective, randomized placebo controlled trial did not show a statistically significant difference between recombinant TGF- β_2 and placebo; consequently, further investigations with TGF- β_2 have been suspended (47).

As bovine TGF- β_2 is expensive and availability is limited, investigators tried other means of delivering a promoter of cellular growth. Although concentration of TGF- β_2 in autologous serum is very low, the possibility that other favourably bioactive cytokines or growth factor may exist prompted its investigation. Several studies subsequent to a pilot study in 11 human eyes, reported anatomic and visual success (48). However, a recent randomized trial has failed to demonstrate a significant beneficial effect of autologous serum (49).

As the alpha granules of platelets contain various growth factors including TGF- β_2 , autologous platelet concentrate has been used as an adjuvant for macular hole surgery. A recent multicentric randomized trial that included 110 eyes reported 94% success rate at 6 months compared to 81% in control group (50).

Thus, only the use of bovine TGF- β_2 and autologous platelets have demonstrated an enhanced anatomic outcome in randomized trials. Bovine- β_2 is not available for human use and autologous platelet preparation requires help of a hematology laboratory.

Although conventional surgery for macular holes is able to achieve a success rate of 80% or more in most cases, the use of biological adjuvants such as autologous platelets significantly improves the hole closure rate. However, the question of the usefulness of adjunctive therapies for macular hole surgery is not well established and a recent survey on macular hole surgery in United States revealed that 80% of surgeons questioned do not believe that adjuvants can be useful (51). It can be argued that adjuvants should be used only in cases with poor prognosis. Failure of prior surgery, re-opening of the hole, long standing holes, traumatic holes or holes in highly myopic eyes would be in this perspective good indication

for the use of adjuvants. They may also help to shorten the duration of face down positioning.

Internal Limiting Membrane Removal in Macular Hole Surgery

The role of internal limiting membrane (ILM) removal in macular hole surgery is currently the subject of a great deal of debate. Morris et al in 1994 had suggested role of ILM removal in all forms of traction maculopathy including macular hole. It was observed, following macular hole surgery, that eyes from which an ERM (52) has been removed had higher success rate compared with eyes that had no detachable ERM. This led to hypothesis that removing the ERM from inner surface of retina (which often includes portions ILM) might mobilize the retina around the macular hole so that it was more flexible and easier to flatten against the underlying retinal pigment epithelium. In a study involving 126 macular hole surgeries, removal of ERM or an absence of an ERM, the presumed ILM was carried out in conjunction with macular hole surgery. Increased success rate in closure of macular holes without adversely affecting the visual results was observed (53).

ILM removal requires modified or novel instrumentation due to extremely thin structure of ILM. Usually a bent MVR blade is used to create a defect in ILM. An ILM elevator is used to elevate the ILM. It is then grasped with either conventional membrane forceps or ILM forceps (Grieshaber). The ILM can be grasped in the inferior and superior part and peeled tangentially or a capsulorrhexis type of peeling can be used to remove a disc shaped patch of ILM off the central macula. A small amount of bleeding often takes place as ILM is lifted off which stops quickly, spontaneously or if infusion bottle is elevated to raise the intraocular pressure.

Fluidic Internal Limiting Membrane Separation (FILMS) technique has also been described in which ILM cannula is used to pierce the ILM and cannulate the sub-ILM space. Viscoelastic is then injected with an injection to elevate the ILM (54).

ILM removal remains controversial because it is technically difficult and may prolong macular surgery. Greater experience will help to define the role of ILM dissection in treatment of macular holes.

Silicone Oil in the treatment of Idiopathic Macular Holes

Long acting gas tamponade (Sulfur hexafluoride or perfluoropropane) is usually used in macular hole surgery. Various studies have stressed on strict face down positioning for 1-2 weeks post operatively as important for staining hole closure (31,55). Certain patients are unable or unwilling to assume a face down position effectively. In such patients use of silicone oil for intraocular tamponade has a role. When silicone oil is used for tamponade, careful attention to achieving as complete a silicone oil fill as possible during the procedure is important in maximising successful results. Patients are asked to maintain a face down position until the morning of the first post-operative day, following which they are instructed only to avoid extended supine positioning. Silicone oil is removed at the patients convenience 4-8 weeks post operatively. The surgical success rate using silicone oil as a tamponade is similar to that in previous reports of surgery using gas (56). With silicone oil, no face down positioning is required and patient can return to near normal activity almost immediately. Specific situations in which surgery with silicone oil might be considered include patients who are unable or unwilling to maintain a post operative face down position, need to return to normal activities in the early post operative period, need to fly or travel to high altitudes, and are monocular and need restoration of visual function as rapidly as possible.

On the other hand, use of silicone oil in macular hole surgery means two surgeries are necessary, one for the initial vitrectomy and one later to remove the oil. This also increases the total expense of the surgery.

Role of Macular Hole Surgery in Impending Macular Holes (Stage 1a and 1b)

In the early stages of macular hole (impending macular holes) patients are asymptomatic or experience mild visual

impairment. Continued traction involving the cortical vitreous results in a full thickness macular defect and corresponding vision loss, where as spontaneous release of vitreous traction can result in subsidence of symptoms. To test the efficacy of prophylactic vitrectomy on impending macular holes, a multicenter, prospective randomized clinical trial was conducted(57). 62 patients were randomly assigned to observation or surgery. The differences between the two groups was not statistically significant so no definitive conclusions could be reached.

Current opinion is vitreous surgery for impending macular holes should not be considered routinely for the following reasons: (1) difficulty in making the correct diagnosis in impending macular holes, (2) unproved benefit, (3) cost and morbidity of surgery, (4) spontaneous recovery in many patients and (5) good anatomic and functional results after macular hole surgery for early full thickness macular holes. But in future with improvement in diagnostic techniques and identification of risk factors and improvement in surgical techniques, a reversal to surgical approach in impending macular holes cannot be ruled out.

Treatment of Persistent or Recurrent Macular Holes

Approximately 10-15% of patients can have failure of macular hole surgery through persistence or recurrence of the hole. Three methods of retreatment for persistent or recurrent macular holes have been reported.

a) First is repeat vitrectomy with membrane dissection and gas fluid exchange. Anatomic success rate following macular hole surgery without adjuvants in persistent and recurrent macular holes is reported to be 87%(58). 80% and 83% success rates have been reported in other studies in which autologous serum and bovine TGF- β_2 were used as adjuncts respectively (59,60).

b) Second method reported is laser photocoagulation followed by gas fluid exchange. Three to six 50 spots of Krypton laser at 0.2 second duration and 90-120 mw are applied to the retina at the border of macular hole using slit lamp delivery system. Another technique is 12-27 spots of yellow laser (50-100mw) are applied at 0.1

second duration and 45-100 mw to the pigment epithelium just inside the border of macular hole, approximately one burn width part, not treating the neurosensory retina. A recent series reported an 87% anatomic success rate(61).

c) Third approach is gas fluid exchange alone. A 74% success rate was noted in patients with persistent holes following vitrectomy.

Though results of anatomic success and visual acuity in all three approaches are similar, vitrectomy with membrane dissection for recurrent holes has the highest single surgery anatomic success rate.

Current opinion is, in persistent holes, if no ILM peeling was done, vitrectomy with ILM peeling is best approach. If ILM peeling was done in persistent hole, any of three approach can be recommended. No compelling evidence is seen for laser, TGF-B₂ or autologous serum as adjuvants. Therefore gas fluid exchange alone or vitrectomy with membrane dissection would be favoured (62).

Complications of Macular Hole Surgery

As experience with macular hole surgery is increasing and long term follow up has become available, post operative complications, as with all procedures are being increasingly recognised. Most of these complications are common to vitrectomy performed for other diseases.

a) Cataract

The most common complication of macular hole surgery is progression of nuclear sclerotic cataract. Studies have reported incidence in the range of 13-95% after vitrectomy for full thickness holes(63).. Altered lens metabolism after vitrectomy is believed to play a role.

b) Glaucoma

The prevalence of IOP increase of more than 30mm Hg after macular hole surgery has ranged from 4% to 39% and most commonly occurs within 2 weeks of surgery(64). The etiology of increased IOP after macular hole surgery is multifactorial including decreased aqueous outflow from post operative inflammation,

shallowing of the anterior chamber with relative angle closure and use of expansile gases and silicone oil for tamponade.

c) Visual field loss

Peripheral visual field loss after macular hole surgery has been recognized only recently with incidence ranging from 7%-16%(65). The pathophysiology of visual field loss is a subject of debate. One hypothesis is inadvertent trauma to the optic nerve with silicone tipped cannula during fluid air exchange or damage to nerve fibre layer during separation of the posterior hyaloid. Another theory is that dessication of the supero temporal retina by the jet of air from inferotemporally placed cannula during fluid air exchange. Additional possibilities include retinal, choroidal or optic nerve ischemia, gas toxicity and light toxicity.

d) Retinal Detachment

Rhegmatogenous retinal detachment is uncommon (1-18%) but potentially serious complication.

e) Retinal pigment epitheliopathy

Severe RPE disturbance with decrease in visual acuity is seen in 11.5% of cases (66).Causative mechanism is multifactorial involving susceptibility to light and resorption of subretinal fluid.

f) Retinal breaks

Iatrogenic retinal breaks are a relatively common complication of macular hole surgery, occurring in 2-17% of cases (67).The majority are peripheral. It is important to carefully examine for retinal breaks prior to fluid air exchange, as small break are overlooked easily when the vitreous cavity is filled with air.

Other complication reported are iatrogenic macular hole, enlargement of macular hole, late reopening of macular hole, retinal dialysis, exudative retinal detachment, branch retinal artery occlusion, endophthalmitis, filaments, anterior ischemic optic neuropathy and choroidalneovascular membrane. Gaining further insight into the mechanisms of these complications may make it possible to further minimise the risks associated with macular hole surgery.

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